

=> fil reg

FILE 'REGISTRY' ENTERED AT 14:05:57 ON 25 AUG 2006

=> d his

FILE 'HCAPLUS' ENTERED AT 12:42:31 ON 25 AUG 2006

L1 1 S US20050009863/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 12:42:52 ON 25 AUG 2006

L2 93 S E1-E93
L3 STR
L4 4 S L3
L5 STR L3
L6 50 S L5
L7 STR L3
L8 STR L7
L9 50 S L8
L10 9243 S L8 FUL
L11 61 S L10 AND L2
SAV L10 DAV781/A
L12 8 S L3 SAM SUB=L10
L13 114 S L3 FUL SUB=L10
L14 17 S L13 AND L2

FILE 'HCAPLUS' ENTERED AT 13:24:59 ON 25 AUG 2006

L15 5 S L13

FILE 'STNGUIDE' ENTERED AT 13:32:20 ON 25 AUG 2006

FILE 'MARPAT' ENTERED AT 13:59:24 ON 25 AUG 2006

L16 0 S L13 SAM
L17 7 S L13 FUL
L18 6 S L17 NOT L15

FILE 'MEDLINE, EMBASE, BIOSIS, CAOLD' ENTERED AT 14:02:04 ON 25
AUG 2006

L19 0 S L13

FILE 'BEILSTEIN' ENTERED AT 14:02:46 ON 25 AUG 2006

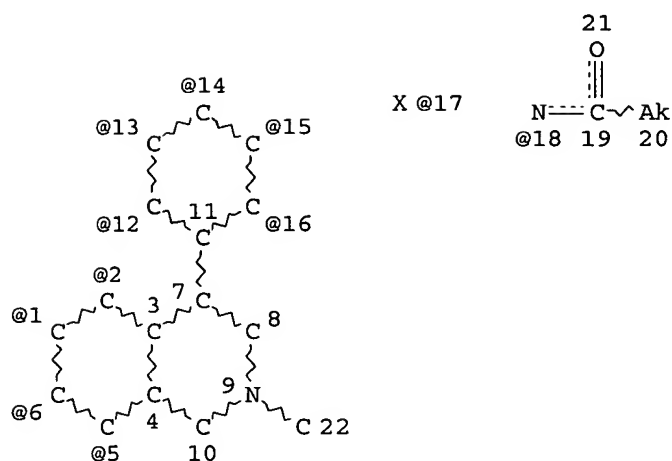
L20 0 S L13 FUL

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=> d que l15

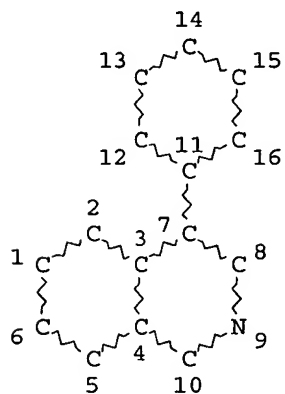
L3 STR



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 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
 L8 STR



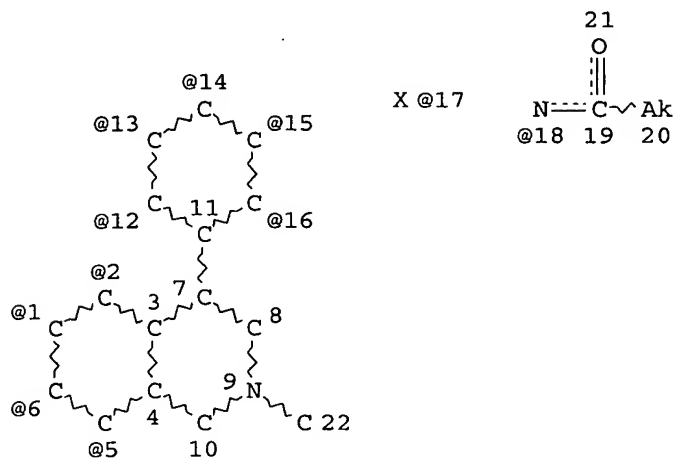
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STEREO ATTRIBUTES: NONE
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 L13 114 SEA FILE=REGISTRY SUB=L10 SSS FUL L3
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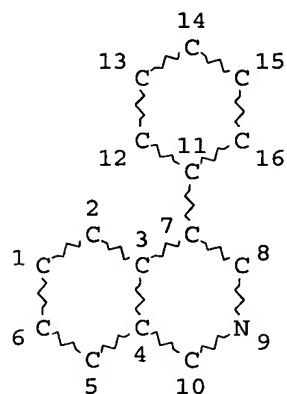
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VPA 17-1/2/5/6 U
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 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
 L8 STR



NODE ATTRIBUTES:
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

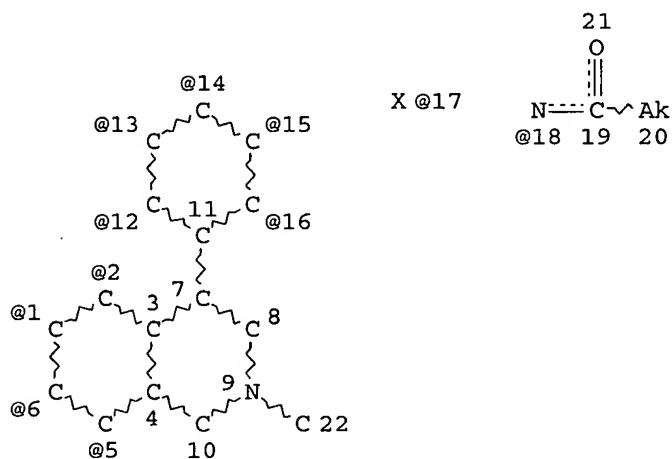
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L17 7 SEA FILE=MARPAT SSS FUL L3
L18 6 SEA FILE=MARPAT ABB=ON L17 NOT L15

=> fil medline biosis embase caold
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FILE 'BIOSIS' ENTERED AT 14:07:17 ON 25 AUG 2006
FILE 'EMBASE' ENTERED AT 14:07:17 ON 25 AUG 2006
FILE 'CAOLD' ENTERED AT 14:07:17 ON 25 AUG 2006

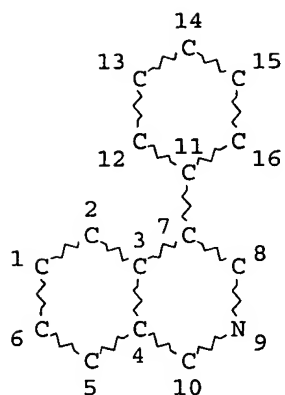
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VPA 18-16/15/14/13/12 U
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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L8 STR



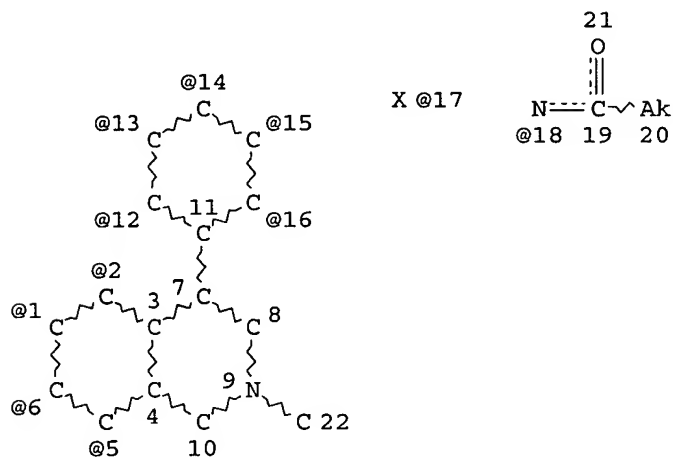
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 DEFAULT MLEVEL IS ATOM
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 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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=> fil beil
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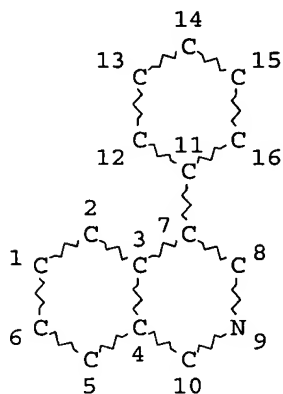


VPA 17-1/2/5/6 U
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L8 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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L13 114 SEA FILE=REGISTRY SUB=L10 SSS FUL L3
L20 0 SEA FILE=BEILSTEIN ABB=ON L13

=> fil hcap
FILE 'HCAPLUS' ENTERED AT 14:07:54 ON 25 AUG 2006

=> d l15 1-5 ibib abs hitstr hitind

L15 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:703445 HCAPLUS
DOCUMENT NUMBER: 145:167104
TITLE: Preparation of 4-phenyltetrahydroisoquinolines
as transport protein NHE-3 inhibitors
INVENTOR(S): Heinelt, Uwe; Lang, Hans-Jochen; Wirth, Klaus;
Licher, Thomas; Hofmeister, Armin
PATENT ASSIGNEE(S): Sanofi-Aventis Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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USHA SHRESTHA EIC 1600 REM 1A64

 WO 2006074813 A1 20060720 WO 2005-EP14127
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 1230
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 CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG,
 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
 KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
 LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
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 SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 DE 102005001411 A1 20060727 DE 2005-102005001411
 2005
 0112
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 2005
 0112

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT
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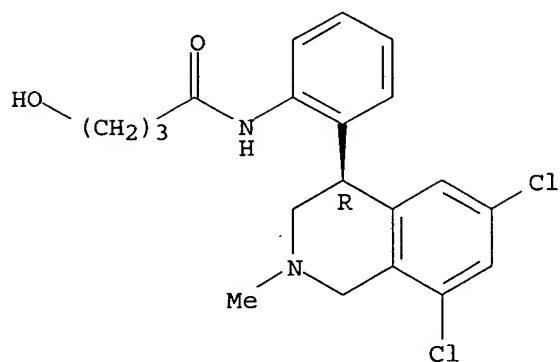
AB The invention relates to the compds. of formula (I), wherein R1 to R8, W, X and Z are defined as in the claims. Title compds. I [R1-R4 = independently H, F, Cl, Br, NO2, NH-CH3, etc.; R5 = H, cyclo/alkyl; R6 = H, OH, F, CF3, cyclo/alkyl; R7, R8 = independently H, F, Br, CO2H and derivs., NH2 and derivs., etc.; W = X = CO, SO2; Z = CO, a bond; and their pharmaceutically acceptable salts] were prepared as transport protein NHE-3 inhibitors. Thus, reacting 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenylamine with Et isocyanatoacetate, followed by cyclization gave tetrahydroisoquinoline II•HCl. In transport protein NHE-3 inhibition assays, 21-examples of compds. I exhibited IC50 values ranging from 0.047-12.3 µM. I are useful for treating renal diseases, such as acute or chronic renal failure, biliary dysfunction and respiratory disorders such as snoring or sleep apnea, etc (no data).

IT 900570-96-9P 900570-97-0P 900571-08-6P
 900571-09-7P 900571-10-0P 900571-13-3P
 (intermediate; preparation of phenyltetrahydroisoquinolines as transport protein NHE-3 inhibitors)

RN 900570-96-9 HCAPLUS

CN Butanamide, N-[2-[(4R)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]-4-hydroxy- (9CI) (CA INDEX NAME)

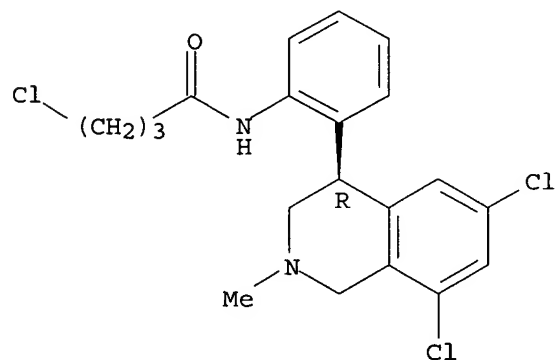
Absolute stereochemistry.



RN 900570-97-0 HCAPLUS

CN Butanamide, 4-chloro-N-[2-[(4R)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)

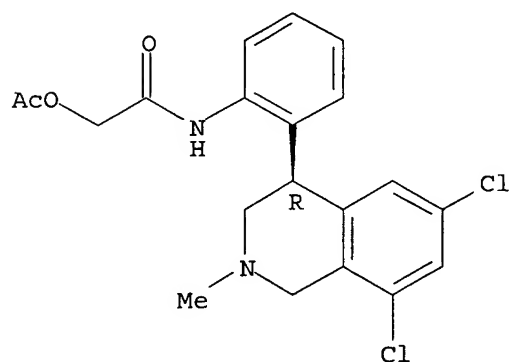
Absolute stereochemistry.



RN 900571-08-6 HCAPLUS

CN INDEX NAME NOT YET ASSIGNED

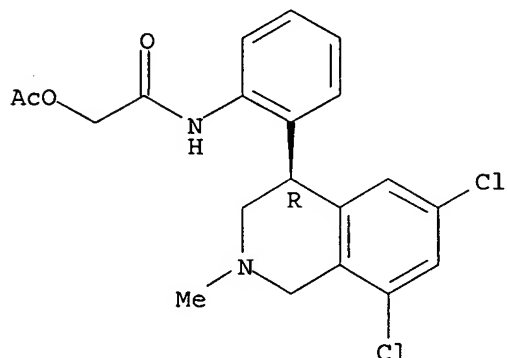
Absolute stereochemistry.



● HCl

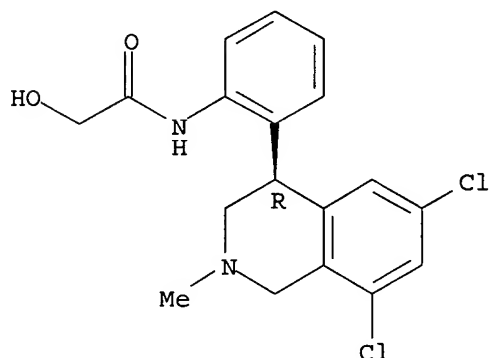
RN 900571-09-7 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 900571-10-0 HCAPLUS
CN Acetamide, N-[2-[(4R)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

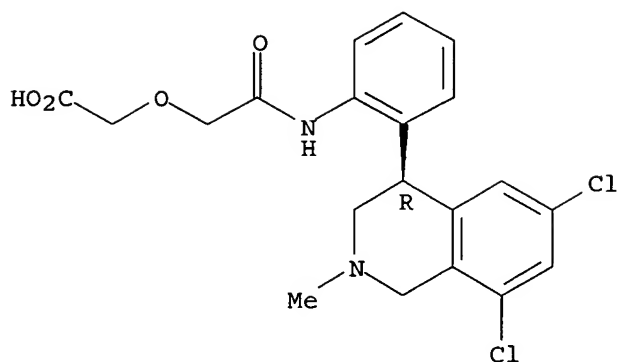


RN 900571-13-3 HCAPLUS
CN Acetic acid, [2-[[2-[(4R)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]amino]-2-oxoethoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 900571-12-2
CMF C20 H20 Cl2 N2 O4

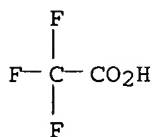
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 33924-45-7P, 2-Bromo-1-bromomethyl-4-chlorobenzene 900570-95-8P,
 [3-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]ureido]acetic acid ethyl ester hydrochloride
 900570-96-9P 900570-97-0P 900570-98-1P
 900570-99-2P 900571-00-8P, 1-(2-Aminophenyl)-2-[cyclopropyl(2,4-dichlorobenzyl)amino]ethanol 900571-07-5P 900571-08-6P
 900571-09-7P 900571-10-0P 900571-13-3P
 900571-14-4P 900571-15-5P 900571-16-6P, N-[2-[2-[(2,4-Dichlorobenzyl)amino]-1-hydroxyethyl]phenyl]acetamide
 900571-17-7P, 1-(2-Aminophenyl)-2-[(2,4-dichlorobenzyl)amino]ethanol 900571-18-8P 900571-19-9P
 900571-24-6P, (2-Bromo-4-chlorobenzyl)methylamine 900571-25-7P,
 N-[2-[2-[(2-Bromo-4-chlorobenzyl)(methyl)amino]acetyl]phenyl]aceta-
 mide 900571-26-8P, N-[2-[2-[(2-Bromo-4-chlorobenzyl)(methyl)amino]-1-hydroxyethyl]phenyl]acetamide
 900571-27-9P, 1-(2-Aminophenyl)-2-[(2-bromo-4-chlorobenzyl)(methyl)amino]ethanol 900571-28-0P,
 2-(8-Bromo-6-chloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenylamine
 (intermediate; preparation of phenyltetrahydroisoquinolines as
 transport protein NHE-3 inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L15 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:292722 HCAPLUS

DOCUMENT NUMBER: 144:350556

TITLE: Preparation of 4-phenyltetrahydroisoquinolines as transport protein NHE-1 inhibitors
 INVENTOR(S): Lang, Hans-Jochen; Heinelt, Uwe; Wirth, Klaus; Licher, Thomas; Hofmeister, Armin
 PATENT ASSIGNEE(S): Sanofi-Aventis Deutschland G.m.b.H., Germany
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006032372	A1	20060330	WO 2005-EP9654	2005 0908

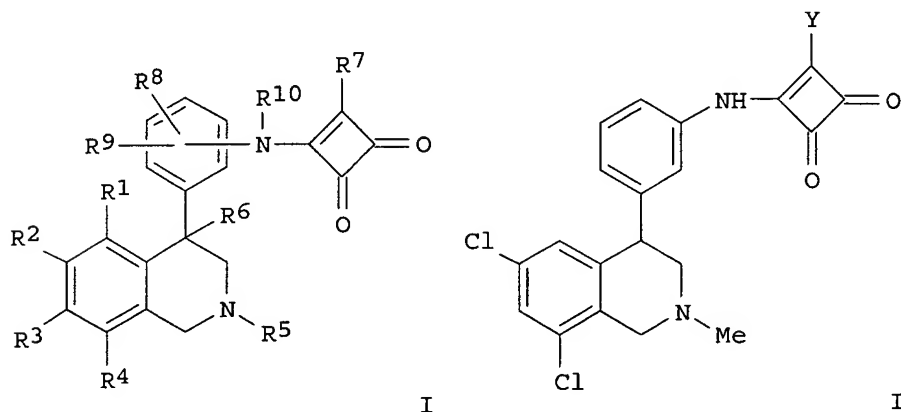
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 DE 102004046492 A1 20060330 DE 2004-102004046492

2004
0923

PRIORITY APPLN. INFO.: DE 2004-102004046492A

2004
0923

OTHER SOURCE(S): MARPAT 144:350556
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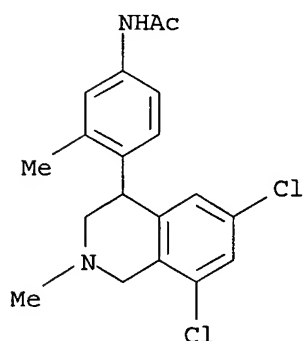


AB Title compds. I [R1, R2, R3, R4 = H, halo, CN, etc.; R5 = H, alkyl, cycloalkyl, etc.; R6 = OH, F, CF3, etc.; R7 = H, alkyl, cycloalkyl, etc.; R8, R9 = H, F, OH, etc.; R10 = H, CH3, CH2CH3] and their pharmaceutically acceptable salts were prepared For example, ammonolysis of cyclobutene II [Y = OEt] afforded claimed phenyltetrahydroisoquinoline II [Y = NH2]. In transport protein NHE-1 inhibition assays, 22-examples of compds. I exhibited IC50 values ranging from 0.031-8.0 μ M.

IT 881315-44-2P
(preparation of phenyltetrahydroisoquinolines as transport protein NHE-1 inhibitors)

RN 881315-44-2 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)-3-methylphenyl]- (9CI) (CA INDEX NAME)



CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 881315-41-9P 881315-44-2P
(preparation of phenyltetrahydroisoquinolines as transport protein NHE-1 inhibitors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L15 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:822748 HCAPLUS

DOCUMENT NUMBER: 141:332066

TITLE: Preparation of 4-phenyltetrahydroisoquinolines
as NHE-3 sodium-proton exchanger inhibitors

INVENTOR(S): Hofmeister, Armin; Heinelt, Uwe; Lang,
Hans-Jochen; Frick, Wendelin; Bleich, Markus;
Wirth, Klaus

PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany

SOURCE: Ger. Offen., 49 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10312963	A1	20041007	DE 2003-10312963	

				2003 0324
AU 2004224242	A1	20041007	AU 2004-224242	
				2004 0311
CA 2519658	AA	20041007	CA 2004-2519658	
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WO 2004085404	A1	20041007	WO 2004-EP2497	
				2004 0311
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PRIORITY APPLN. INFO.:			DE 2003-10312963	A
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OTHER SOURCE(S):	MARPAT 141:332066			
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT

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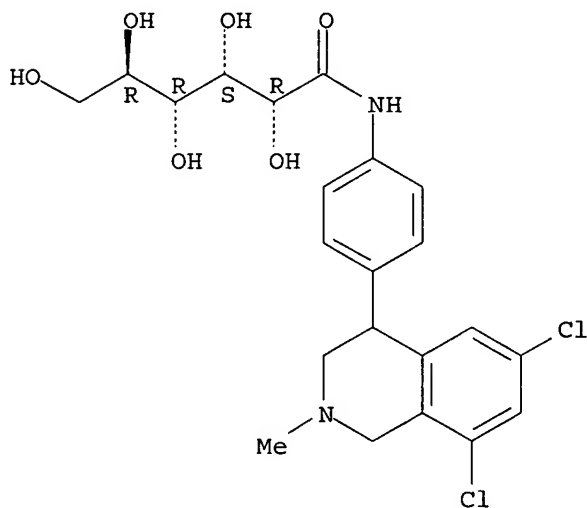
AB Title compds. I [R1, R2, R3, R4 = H, halo, CN, etc.; R5 = H, alkyl, cycloalkyl, etc.; R6 = H, OH, halo, etc.; R7, R8, R9 = CH2, O, OCO, etc.;] and their pharmaceutically acceptable salts were prepared. For example, N-acylation of aniline II, e.g., prepared from 2,4-dichlorobenzylmethylamine in 5-steps, with penta-O-acetyl-D-gluconoyl chloride, followed by acetate hydrolysis, afforded claimed isoquinoline III. In NHE-3 sodium-proton exchanger inhibition assays, 4-examples of compds. I exhibited IC50 values ranging from 0.0036-0.1594 μ M. Compds. I are claimed useful for the treatment of acute or chronic kidney failure.

IT 771576-93-3P 771576-94-4P 771576-95-5P
 771576-96-6P 771576-97-7P 771576-98-8P
 771577-24-3P 771577-25-4P 771577-26-5P
 771577-28-7P 771577-34-5P 771578-00-8P
 (preparation of phenyltetrahydroisoquinolines as NHE-3 sodium-proton exchanger inhibitors)

RN 771576-93-3 HCAPLUS

CN D-Gluconamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)

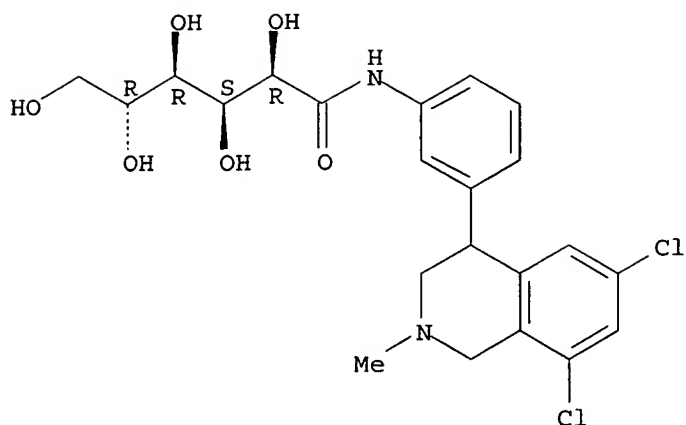
Absolute stereochemistry.



RN 771576-94-4 HCAPLUS

CN D-Gluconamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)

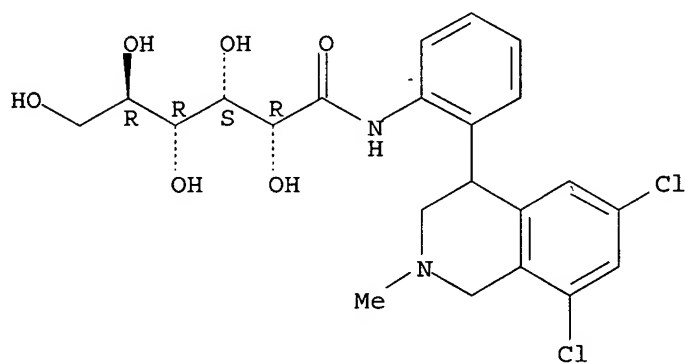
Absolute stereochemistry.



RN 771576-95-5 HCAPLUS

CN D-Gluconamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)

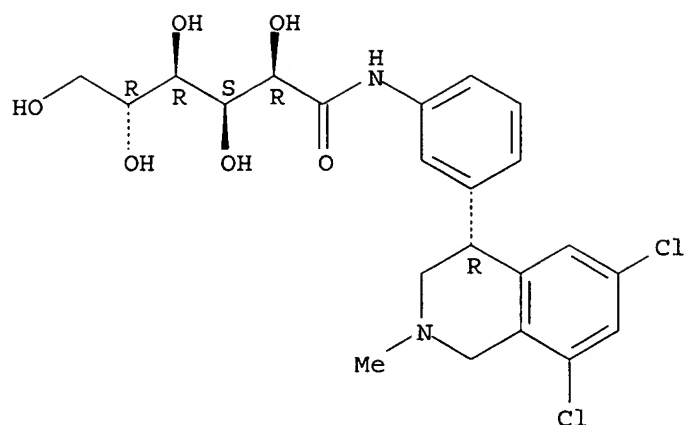
Absolute stereochemistry.



RN 771576-96-6 HCAPLUS

CN D-Gluconamide, N-[3-[(4R)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)

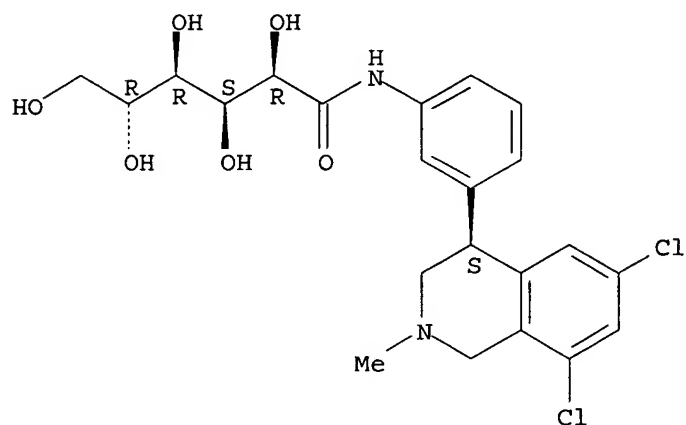
Absolute stereochemistry.



RN 771576-97-7 HCAPLUS

CN D-Gluconamide, N-[3-[(4S)-6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)

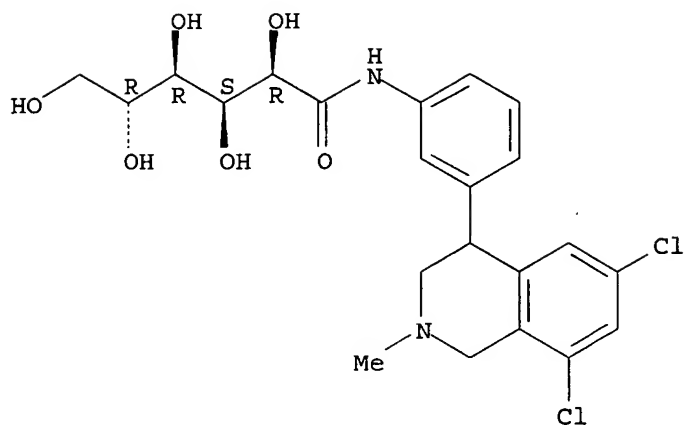
Absolute stereochemistry.



RN 771576-98-8 HCAPLUS

CN D-Gluconamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

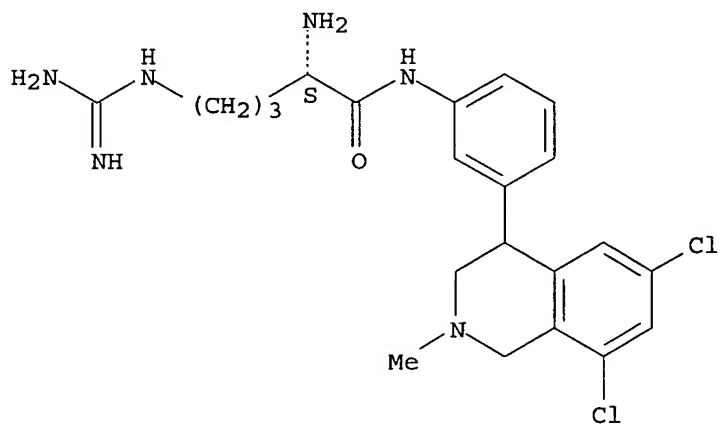


● HCl

RN 771577-24-3 HCAPLUS

CN Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

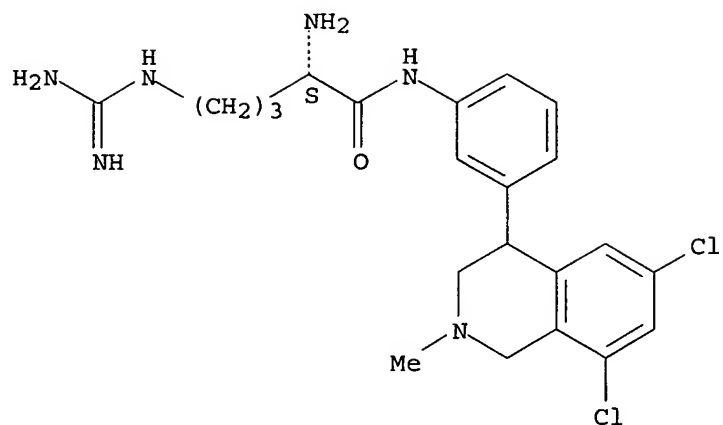


● HCl

RN 771577-25-4 HCAPLUS

CN Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-(9CI) (CA INDEX NAME)

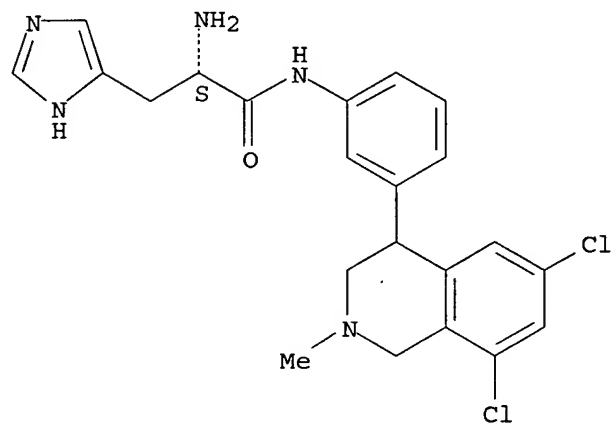
Absolute stereochemistry.



RN 771577-26-5 HCAPLUS

CN 1H-Imidazole-4-propanamide, α-amino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (αS)-(9CI) (CA INDEX NAME)

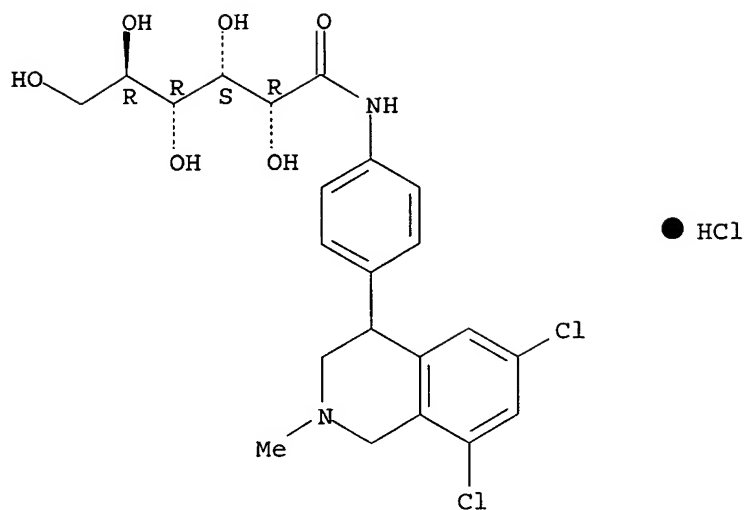
Absolute stereochemistry.



RN 771577-28-7 HCAPLUS

CN D-Gluconamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

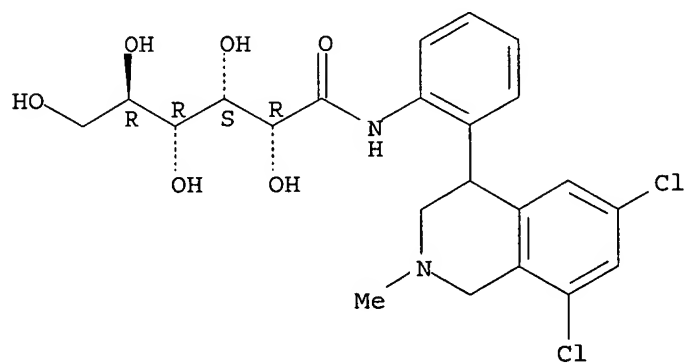
Absolute stereochemistry.



RN 771577-34-5 HCAPLUS

CN D-Gluconamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

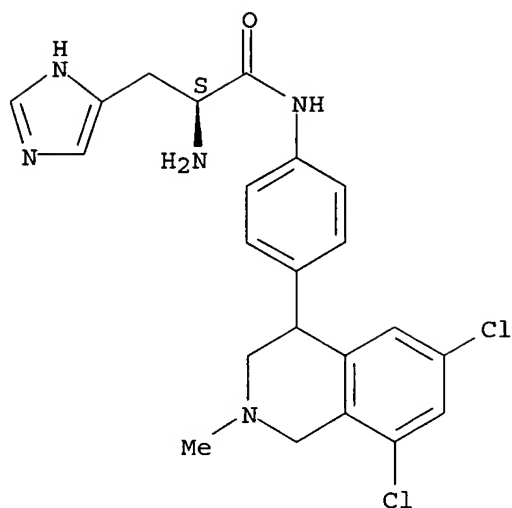
Absolute stereochemistry.



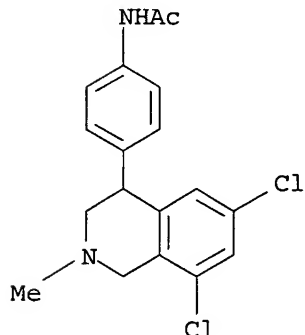
RN 771578-00-8 HCAPLUS

CN 1H-Imidazole-4-propanamide, α -amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (α S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

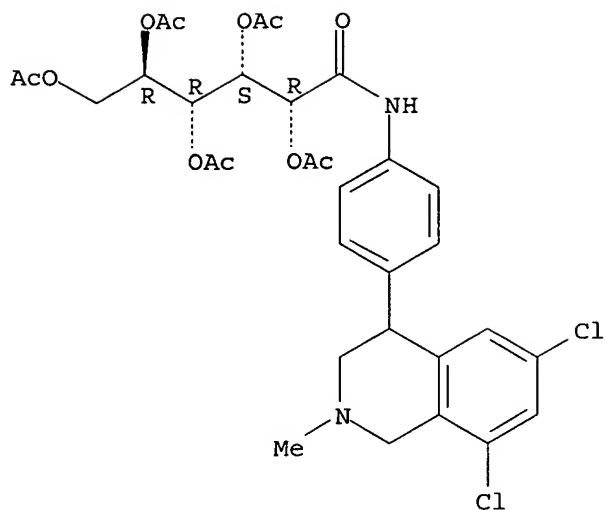


IT 543734-46-9P 771577-27-6P 771577-29-8P
 771577-33-4P 771577-55-0P
 (preparation of phenyltetrahydroisoquinolines as NHE-3 sodium-proton
 exchanger inhibitors)
 RN 543734-46-9 HCAPLUS
 CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-
 isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 771577-27-6 HCAPLUS
 CN D-Gluconamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-
 isoquinolinyl)phenyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX
 NAME)

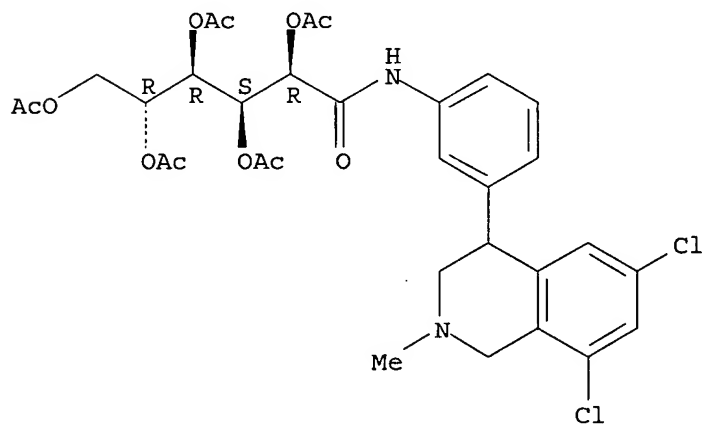
Absolute stereochemistry.



RN 771577-29-8 HCAPLUS

CN D-Gluconamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

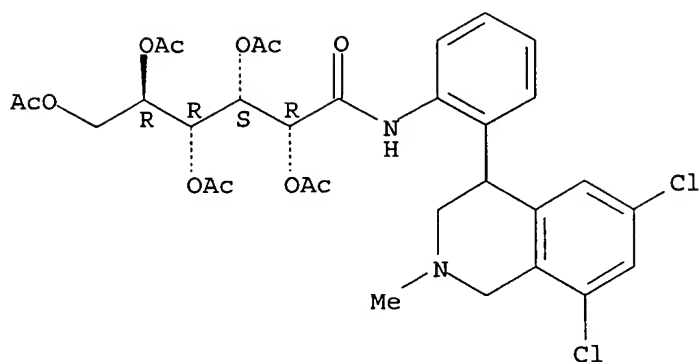
Absolute stereochemistry.



RN 771577-33-4 HCAPLUS

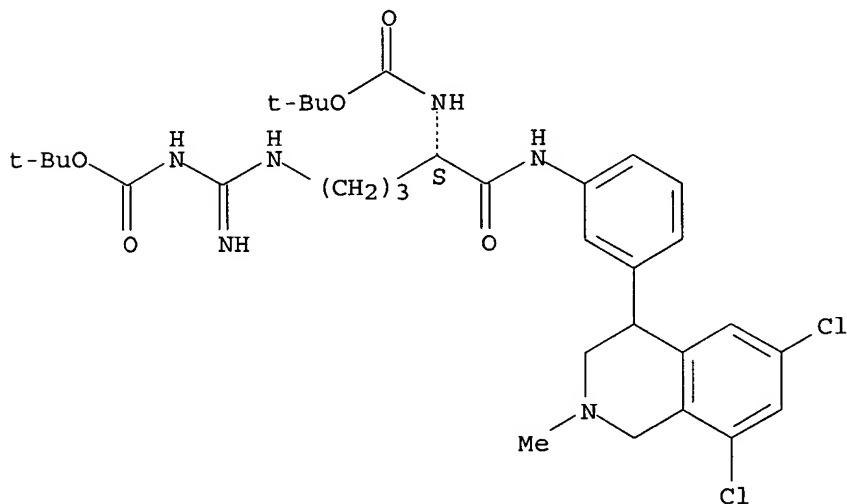
CN D-Gluconamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 771577-55-0 HCAPLUS
 CN 11-Oxa-2,4,9-triazatridecanoic acid, 8-[[[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]amino]carbonyl]-3-imino-12,12-dimethyl-10-oxo-, 1,1-dimethylethyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D217-14
 ICS C07D401-12; A61K031-47; A61P013-00
 CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 IT 771576-93-3P 771576-94-4P 771576-95-5P
 771576-96-6P 771576-97-7P 771576-98-8P
 771576-99-9P 771577-00-5P 771577-01-6P 771577-02-7P
 771577-03-8P 771577-04-9P 771577-05-0P 771577-06-1P
 771577-07-2P 771577-08-3P 771577-09-4P 771577-10-7P
 771577-11-8P 771577-12-9P 771577-13-0P 771577-14-1P
 771577-15-2P 771577-16-3P 771577-17-4P 771577-18-5P
 771577-19-6P 771577-20-9P 771577-21-0P 771577-22-1P
 771577-23-2P 771577-24-3P 771577-25-4P
 771577-26-5P 771577-28-7P 771577-34-5P
 771577-35-6P 771577-36-7P 771577-37-8P 771577-39-0P
 771577-41-4P 771578-00-8P

(preparation of phenyltetrahydroisoquinolines as NHE-3 sodium-proton exchanger inhibitors)

IT 4688-64-6P, N-[2-(2-Bromoacetyl)phenyl]acetamide 21675-02-5P,
N-[4-(2-Bromoacetyl)phenyl]acetamide 30071-93-3P,
1-[3,5-Bis(trifluoromethyl)phenyl]ethanone 131805-94-2P,
1-[3,5-Bis(trifluoromethyl)phenyl]-2-bromoethanone
543734-46-9P 543734-76-5P 543735-10-0P 543737-13-9P,
3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzoic acid 543739-85-1P 771577-27-6P
771577-29-8P 771577-30-1P 771577-31-2P 771577-32-3P
771577-33-4P 771577-38-9P 771577-40-3P 771577-43-6P
771577-44-7P 771577-46-9P 771577-47-0P, (R)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenylamine
771577-48-1P, (S)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenylamine 771577-49-2P
771577-50-5P 771577-51-6P 771577-53-8P 771577-55-0P

(preparation of phenyltetrahydroisoquinolines as NHE-3 sodium-proton exchanger inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L15 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:506576 HCAPLUS

DOCUMENT NUMBER: 139:69164

TITLE: Preparation of substituted
4-phenyltetrahydroisochinolinium salts as
inhibitors of cellular sodium-proton
antiporters

INVENTOR(S): Hofmeister, Armin; Lang, Hans-Jochen; Heinelt,
Uwe; Bleich, Markus; Wirth, Klaus

PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany

SOURCE: Ger. Offen., 16 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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DE 10163914	A1	20030703	DE 2001-10163914	2001 1222
CA 2471217	AA	20030710	CA 2002-2471217	2002 1209
WO 2003055880	A2	20030710	WO 2002-EP13922	2002 1209
WO 2003055880	A3	20031106		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,			

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
 SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
 ML, MR, NE, SN, TD, TG

AU 2002361028 A1 20030715 AU 2002-361028 2002
 1209

EP 1465870 A2 20041013 EP 2002-795126 2002
 1209

EP 1465870 B1 20060503
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,
 EE, SK

JP 2005524616 T2 20050818 JP 2003-556410 2002
 1209

AT 325100 E 20060615 AT 2002-795126 2002
 1209

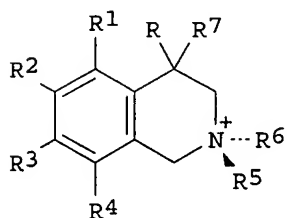
US 2003171580 A1 20030911 US 2002-324041 2002
 1220

US 6703405 B2 20040309
 PRIORITY APPLN. INFO.: DE 2001-10163914 A 2001
 1222

US 2002-353614P P 2002
 0201

WO 2002-EP13922 W 2002
 1209

OTHER SOURCE(S): MARPAT 139:69164
 GI



I

AB 4-Phenyltetrahydroisochinolinium salts I [substituted Ph; R1-R4 = H, F, Cl, I, Br, CN, NO2, (un)substituted alkyl, alkoxy, alkoxy carbonyl, acyloxy, acyl, OPh, phenylalkoxy, heteroaryl, CONH2, OH, NH2, R5, R6 = (un)substituted alkyl; NR5R6 = heterocyclic; R7 = H, F, Cl, Br, I, (un)substituted alkyl, alkoxy, acyloxy; Y = F, Cl, Br, I, OH, carboxylic sulfonic acid anion] were prepared. They are inhibitors of the cellular sodium proton antiporters. They affect the serum lipoproteins and can therefore be used for the prophylaxis and treatment of atherosclerotic

conditions. Thus, 2,4-Cl₂C₆H₃CH₂NH₂ was treated with BrCH₂COPh to give 2,4-Cl₂C₆H₃CH₂NHCH₂COPh, which was reduced to the alc., cyclized, and quaternized to give I [R = Ph, R₁, R₃ = H, R₂, R₄ = Cl, R₅, R₆ = Me; Y = CF₃CO₂] which had an IC₅₀ for inhibition of the sodium-proton exchanger NHE3.

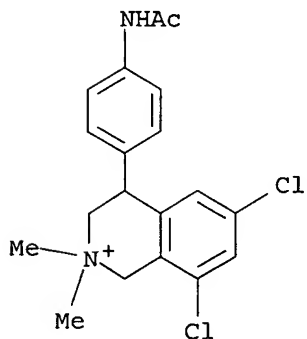
IT 552290-31-0P 552290-32-1P 552290-33-2P

552290-34-3P 552290-35-4P

(preparation of substituted 4-phenyltetrahydroisochinolinium salts as inhibitors of cellular sodium-proton antiporters)

RN 552290-31-0 HCAPLUS

CN Isoquinolinium, 4-[4-(acetylamino)phenyl]-6,8-dichloro-1,2,3,4-tetrahydro-2,2-dimethyl-, iodide (9CI) (CA INDEX NAME)

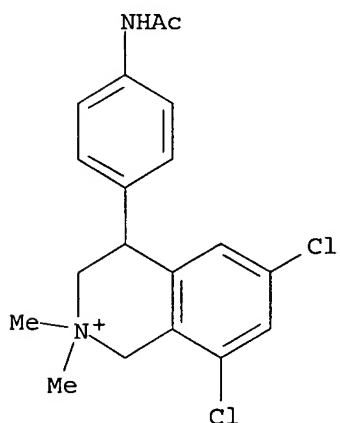


● I⁻

RN 552290-32-1 HCAPLUS

CN Isoquinolinium, 4-[4-(acetylamino)phenyl]-6,8-dichloro-1,2,3,4-tetrahydro-2,2-dimethyl-, iodide, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

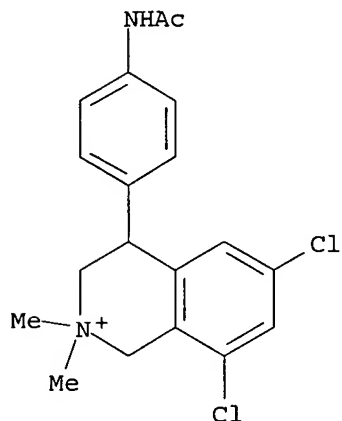


● I⁻

RN 552290-33-2 HCAPLUS

CN Isoquinolinium, 4-[4-(acetylamino)phenyl]-6,8-dichloro-1,2,3,4-tetrahydro-2,2-dimethyl-, chloride, (+)- (9CI) (CA INDEX NAME)

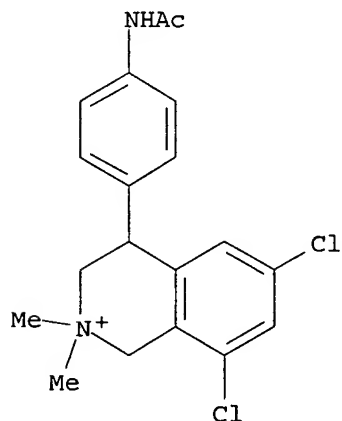
Rotation (+).

● Cl⁻

RN 552290-34-3 HCAPLUS

CN Isoquinolinium, 4-[4-(acetylamino)phenyl]-6,8-dichloro-1,2,3,4-tetrahydro-2,2-dimethyl-, iodide, (-)- (9CI) (CA INDEX NAME)

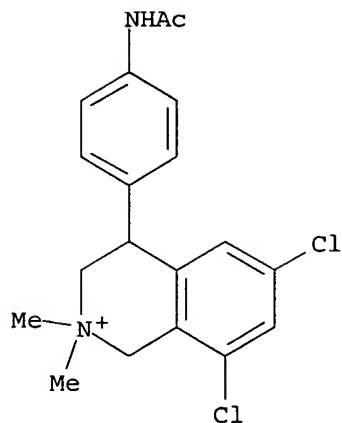
Rotation (-).

● I⁻

RN 552290-35-4 HCAPLUS

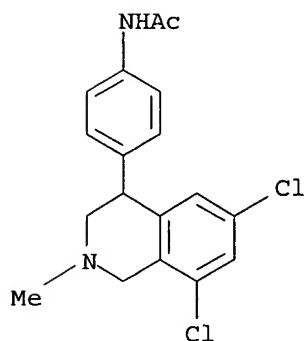
CN Isoquinolinium, 4-[4-(acetylamino)phenyl]-6,8-dichloro-1,2,3,4-tetrahydro-2,2-dimethyl-, chloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



● Cl⁻

IT 543734-46-9P
 (preparation of substituted 4-phenyltetrahydroisochinolinium salts
 as inhibitors of cellular sodium-proton antiporters)
 RN 543734-46-9 HCAPLUS
 CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-
 isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



IC ICM C07D217-04
 ICS A61K031-47
 CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 11
 IT 552290-27-4P 552290-30-9P 552290-31-0P
 552290-32-1P 552290-33-2P 552290-34-3P
 552290-35-4P
 (preparation of substituted 4-phenyltetrahydroisochinolinium salts
 as inhibitors of cellular sodium-proton antiporters)
 IT 543734-46-9P 543734-48-1P 543737-21-9P,
 6,8-Dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline
 543738-38-1P 543739-86-2P, 2-[(2,4-Dichlorobenzyl)-N-
 methylamino]-1-phenylethanone 543739-87-3P, 2-[(2,4-
 Dichlorobenzyl)-N-methylamino]-1-phenylethanol 552290-36-5P
 552290-37-6P
 (preparation of substituted 4-phenyltetrahydroisochinolinium salts
 as inhibitors of cellular sodium-proton antiporters)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L15 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:454295 HCAPLUS

DOCUMENT NUMBER: 139:52892

TITLE: Preparation of 2-(2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyls as sodium ion proton antiporter (NHE) inhibitors

INVENTOR(S): Hofmeister, Armin; Heinelt, Uwe; Lang, Hans-Jochen; Bleich, Markus; Wirth, Klaus; Gekle, Michael

PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany

SOURCE: PCT Int. Appl., 304 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048129	A1	20030612	WO 2002-EP12990	2002 1120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2469385	AA	20030612	CA 2002-2469385	2002 1120
AU 2002356689	A1	20030617	AU 2002-356689	2002 1120
EP 1453810	A1	20040908	EP 2002-804183	2002 1120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014753	A	20041214	BR 2002-14753	2002 1120
CN 1617856	A	20050518	CN 2002-827887	2002 1120
JP 2005515205	T2	20050526	JP 2003-549321	2002 1120

US 2004044211	A1	20040304	US 2002-309352	2002 1204
US 6911453	B2	20050628		
ZA 2004003711	A	20050609	ZA 2004-3711	2004 0514
NO 2004002158	A	20040827	NO 2004-2158	2004 0525
US 2005009864	A1	20050113	US 2004-866843	2004 0614
PRIORITY APPLN. INFO.:			DE 2001-10159714	A 2001 1205
			US 2002-353513P	P 2002 0201
			WO 2002-EP12990	W 2002 1120
			US 2002-309352	A3 2002 1204

OTHER SOURCE(S): MARPAT 139:52892
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT
*

AB Title compds. I [R1, R2, R3, R4 = H, halo, CN, etc.; R5 = H, C₆H₂p+1, C₅H₂ss-1, etc.; p = 1-8; ss = 3-8; R6 = H, halo, OH, etc.; R7, R8, R9 = Ov-SOw-R23; v = 0, 1; w = 0-2, R23 = OH, C₆H₂nn+1, C₆H₂mm-1, etc.; nn = 1-8] and their pharmaceutically acceptable salts were prepared For example, acid catalyzed intramol. Pictet Spengler cyclization of benzyl alc. II, prepared from N-methyl-2,4-dichlorobenzylamine in 3-steps, afforded claimed phenyltetrahydroisoquinoline III. In proton sodium antiporting protein (NHE3) inhibition studies, 27-examples of compds. I exhibited IC₅₀ values ranging from 0.024-1.507 μ M, e.g., the IC₅₀ value of phenyltetrahydroisoquinoline III hydrochloride was 0.075 μ M. Compds. I can also influence serum lipoproteins and can be used for the regression of atherosclerotic alterations.

IT 543734-46-9P, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]acetamide 543734-88-9P, N-[4-(6-Bromo-8-chloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]acetamide 543734-90-3P 543734-92-5P 543734-94-7P, N-[4-[8-Chloro-2-methyl-6-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl]phenyl]acetamide 543734-96-9P, N-[4-[8-Chloro-6-(cyclopropylmethylamino)-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl]phenyl]acetamide 543735-07-5P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-

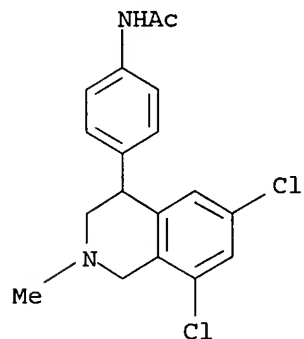
tetrahydroisoquinolin-4-yl)phenyl]acetamide 543735-12-2P
, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]propionamide 543735-14-4P,
N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]butyramide 543735-16-6P, Pentanoic
acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543735-17-7P, N-[4-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isobutyramide 543735-19-9P, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-2,2-dimethylpropionamide 543735-27-9P 543735-39-3P, N-[3-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]propionamide 543735-41-7P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]butyramide 543735-42-8P
, Pentanoic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-44-0P,
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isobutyramide 543735-46-2P,
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2,2-dimethylpropionamide 543735-54-2P
543735-64-4P, N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]propionamide 543735-66-6P, N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]butyramide 543735-68-8P
, Pentanoic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-69-9P
543735-71-3P, N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-2,2-dimethylpropionamide 543735-76-8P 543736-00-1P, 2-Amino-N-[4-(6,8-
dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]acetamide 543736-01-2P, N-[4-(6,8-Dichloro-2-
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methylaminoacetamide 543736-02-3P, N-[4-(6,8-Dichloro-2-
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dimethylaminoacetamide 543736-03-4P,
2-Amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]propionamide 543736-04-5P,
2-Amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]butyramide 543736-05-6P, 2,6-Diaminohexanoic
acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-19-2P, N-[3-(6,8-Dichloro-2-
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methylaminoacetamide 543736-20-5P, N-[3-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2-
dimethylaminoacetamide 543736-21-6P,
2-Amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]propionamide 543736-22-7P,
2-Amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]butyramide 543736-23-8P, 2,6-Diaminohexanoic
acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543737-09-3P, N-[3-(6,8-Difluoro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]acetamide 543737-44-6P 543737-65-1P 543737-66-2P
543737-71-9P 543737-72-0P 543737-73-1P
543737-74-2P 543737-79-7P 543737-80-0P
543737-81-1P 543737-82-2P 543737-83-3P
543737-90-2P 543737-91-3P 543737-92-4P
543737-93-5P 543737-94-6P 543737-98-0P
543738-04-1P 543738-05-2P 543738-06-3P
543738-07-4P 543738-08-5P 543738-12-1P

543738-23-4P 543738-24-5P 543738-52-9P
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 543738-58-5P 543738-60-9P 543738-75-6P
 543738-76-7P 543738-78-9P 543738-80-3P
 543738-82-5P 543739-80-6P 543739-83-9P

(drug candidate; preparation of phenyltetrahydroisoquinolines as sodium ion proton antiporter inhibitors)

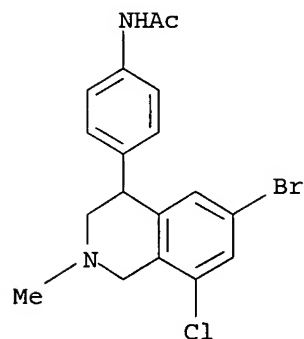
RN 543734-46-9 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



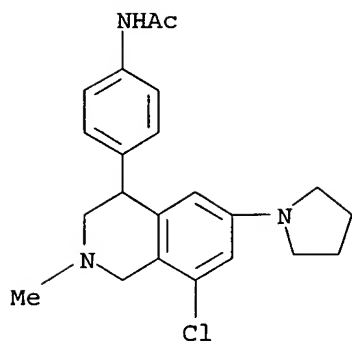
RN 543734-88-9 HCAPLUS

CN Acetamide, N-[4-(6-bromo-8-chloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



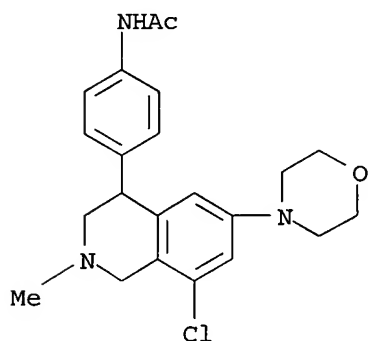
RN 543734-90-3 HCAPLUS

CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(1-pyrrolidinyl)-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)



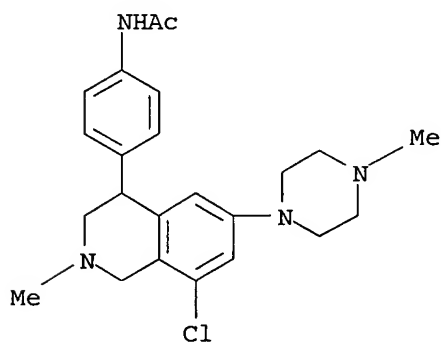
RN 543734-92-5 HCAPLUS

CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(4-morpholinyl)-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)



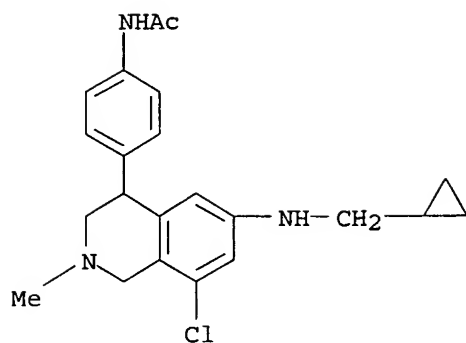
RN 543734-94-7 HCAPLUS

CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(4-methyl-1-piperazinyl)-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)



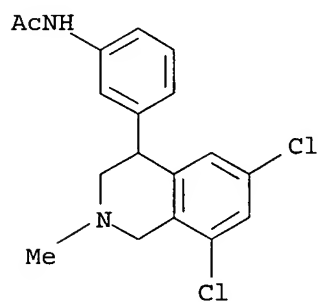
RN 543734-96-9 HCAPLUS

CN Acetamide, N-[4-[8-chloro-6-[(cyclopropylmethyl)amino]-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]- (9CI) (CA INDEX NAME)



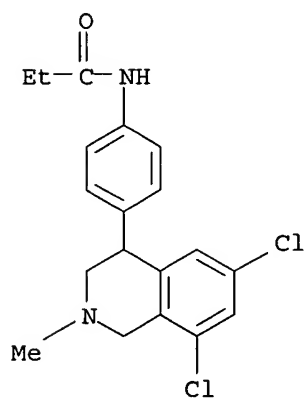
RN 543735-07-5 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



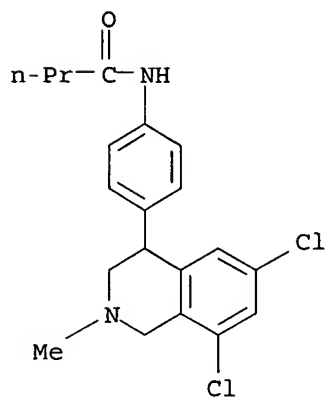
RN 543735-12-2 HCAPLUS

CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



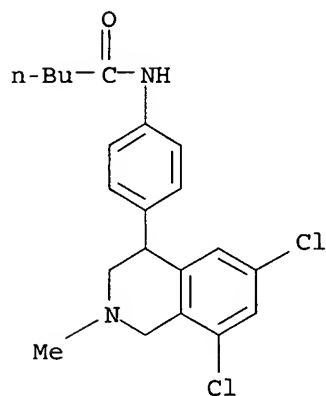
RN 543735-14-4 HCAPLUS

CN Butanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



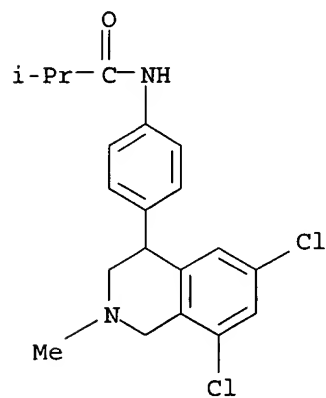
RN 543735-16-6 HCAPLUS

CN Pentanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



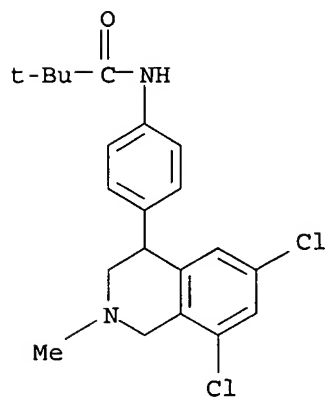
RN 543735-17-7 HCAPLUS

CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl- (9CI) (CA INDEX NAME)



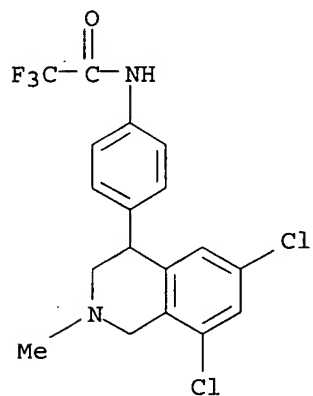
RN 543735-19-9 HCAPLUS

CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



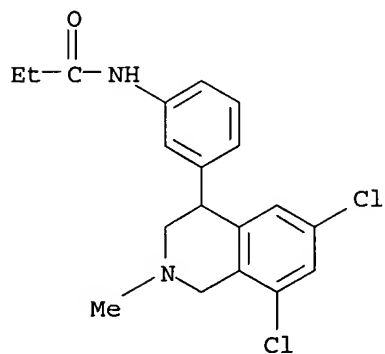
RN 543735-27-9 HCAPLUS

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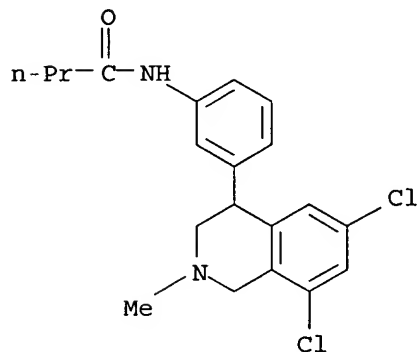
RN 543735-39-3 HCAPLUS

CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



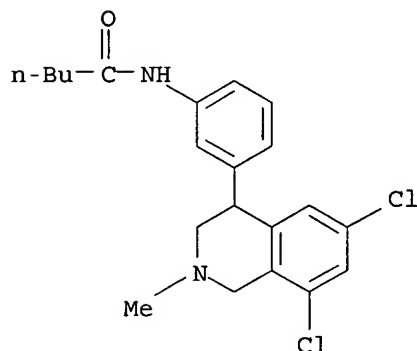
RN 543735-41-7 HCAPLUS

CN Butanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



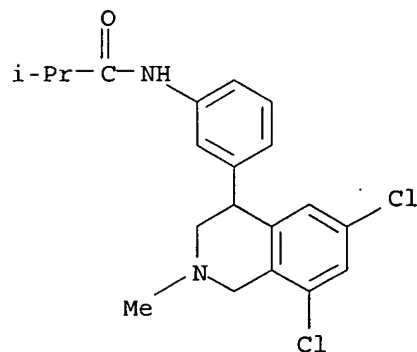
RN 543735-42-8 HCAPLUS

CN Pentanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)

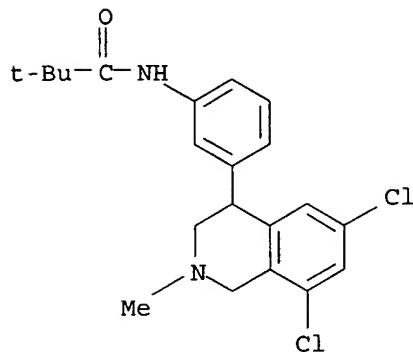


RN 543735-44-0 HCAPLUS

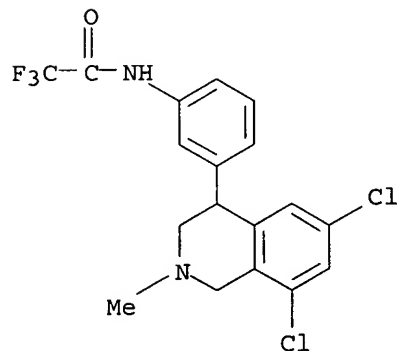
CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl- (9CI) (CA INDEX NAME)



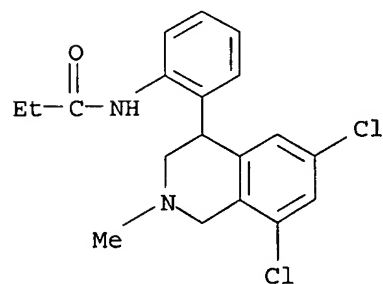
RN 543735-46-2 HCAPLUS
CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 543735-54-2 HCAPLUS
CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)

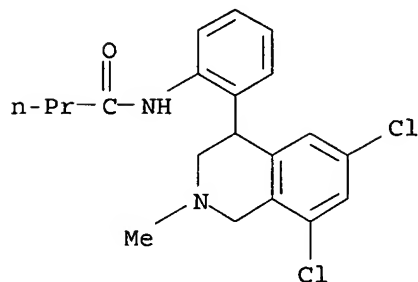


RN 543735-64-4 HCAPLUS
CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



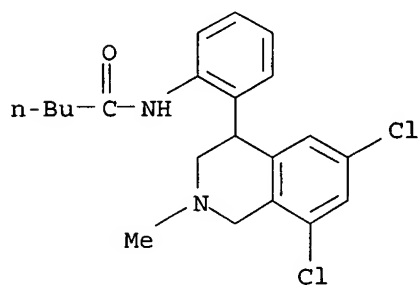
RN 543735-66-6 HCAPLUS
CN Butanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-

isoquinolinyl)phenyl] - (9CI) (CA INDEX NAME)



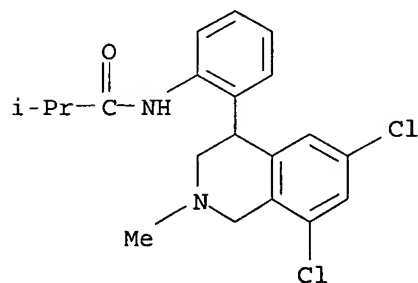
RN 543735-68-8 HCAPLUS

CN Pentanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl] - (9CI) (CA INDEX NAME)



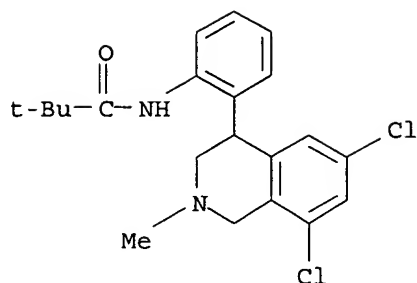
RN 543735-69-9 HCAPLUS

CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl- (9CI) (CA INDEX NAME)



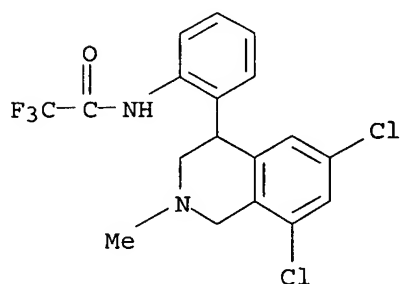
RN 543735-71-3 HCAPLUS

CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



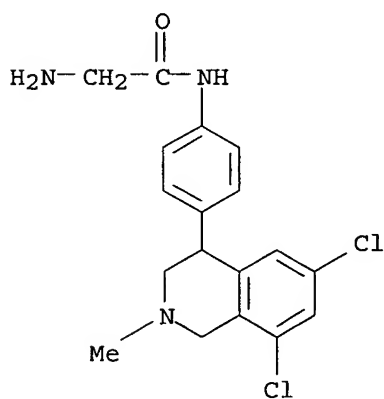
RN 543735-76-8 HCAPLUS

CN Acetamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)



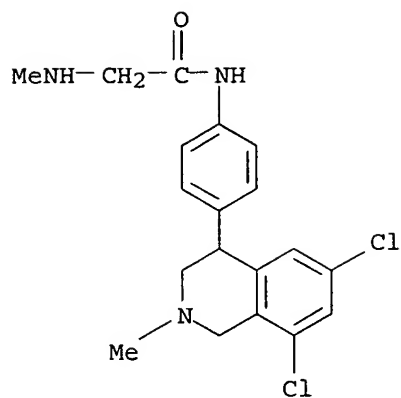
RN 543736-00-1 HCAPLUS

CN Acetamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



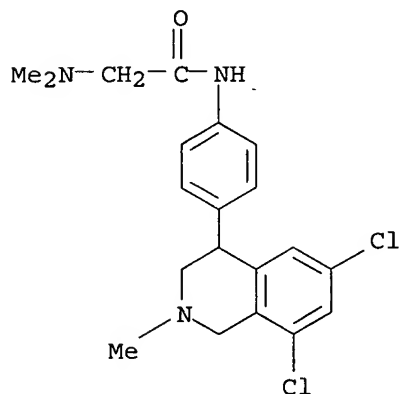
RN 543736-01-2 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(methylamino)- (9CI) (CA INDEX NAME)



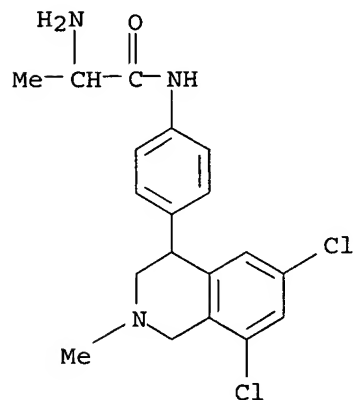
RN 543736-02-3 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(dimethylamino)- (9CI) (CA INDEX NAME)



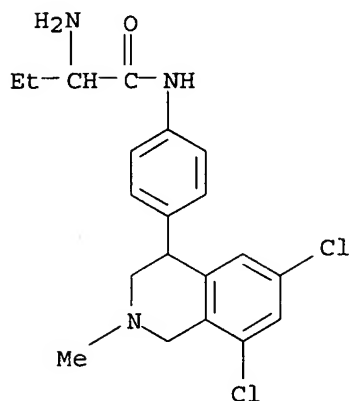
RN 543736-03-4 HCAPLUS

CN Propanamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



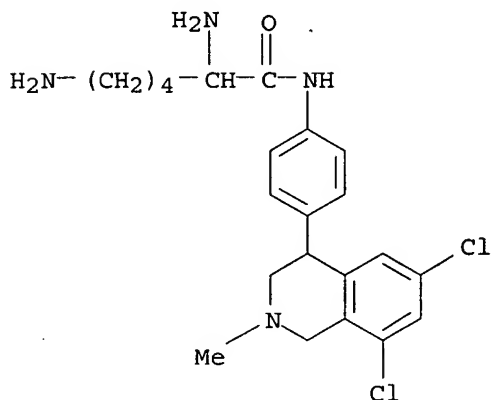
RN 543736-04-5 HCAPLUS

CN Butanamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



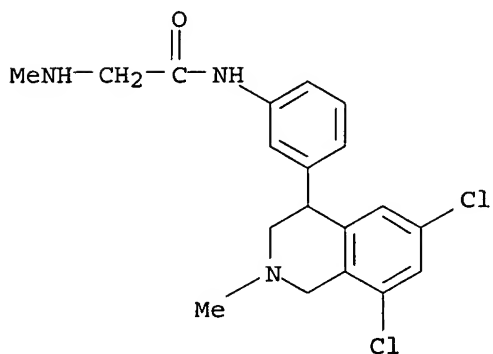
RN 543736-05-6 HCAPLUS

CN Hexanamide, 2,6-diamino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



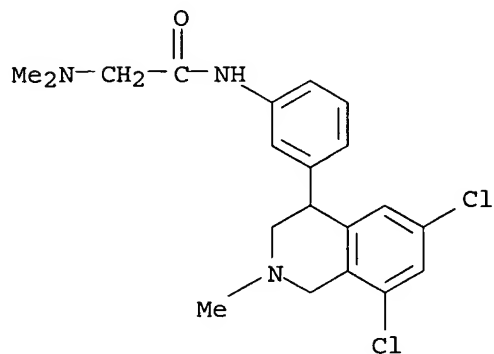
RN 543736-19-2 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(methylamino)- (9CI) (CA INDEX NAME)



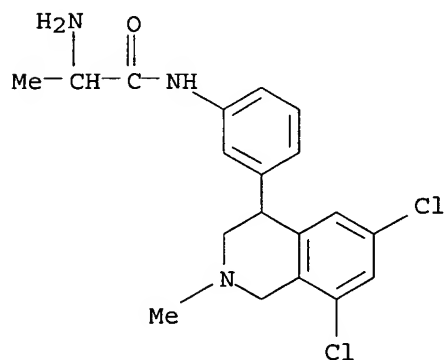
RN 543736-20-5 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(dimethylamino)- (9CI) (CA INDEX NAME)



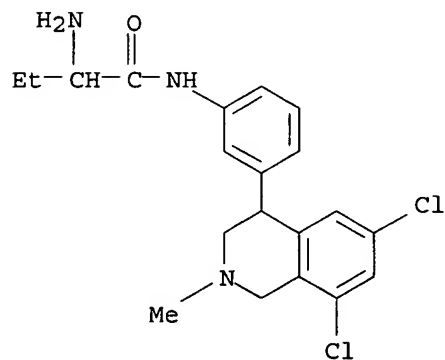
RN 543736-21-6 HCAPLUS

CN Propanamide, 2-amino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



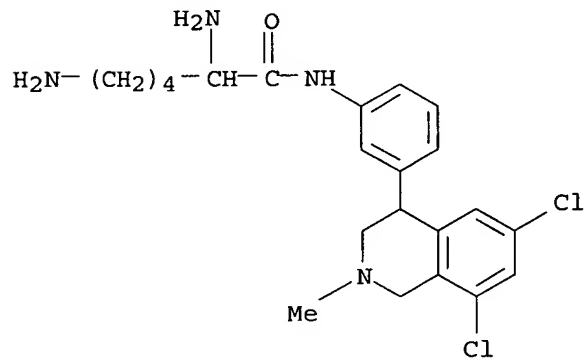
RN 543736-22-7 HCAPLUS

CN Butanamide, 2-amino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



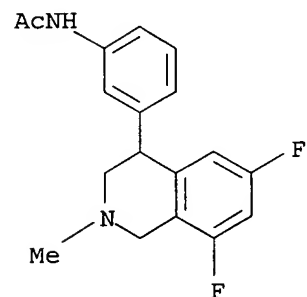
RN 543736-23-8 HCAPLUS

CN Hexanamide, 2,6-diamino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



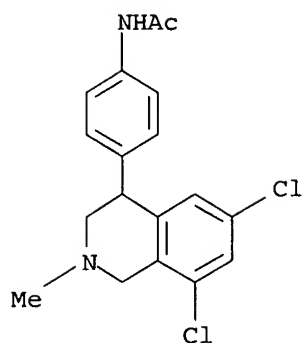
RN 543737-09-3 HCAPLUS

CN Acetamide, N-[3-(6,8-difluoro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 543737-44-6 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

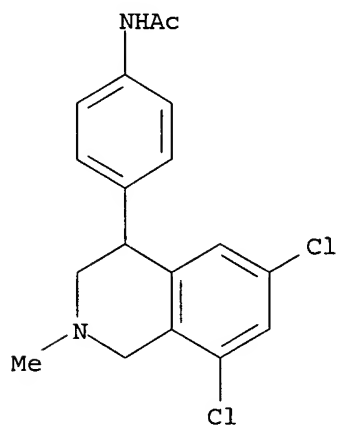


● HCl

RN 543737-65-1 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (-)- (9CI) (CA INDEX NAME)

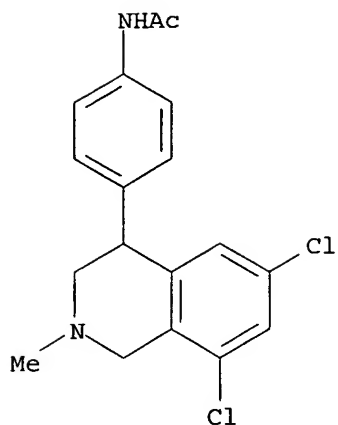
Rotation (-).



RN 543737-66-2 HCAPLUS

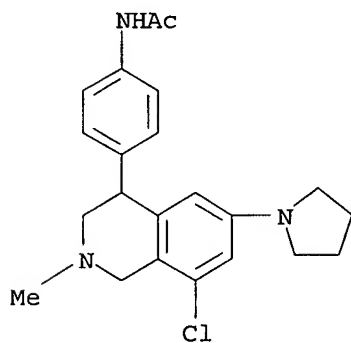
CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 543737-71-9 HCAPLUS

CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(1-pyrrolidinyl)-4-isoquinolinyl]phenyl]-, monohydrochloride (9CI)
(CA INDEX NAME)



● HCl

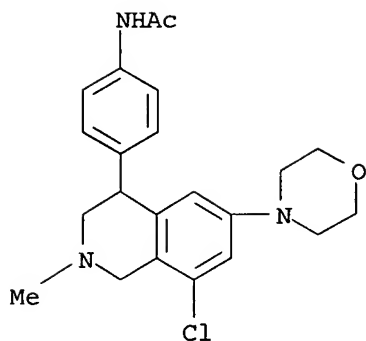
RN 543737-72-0 HCAPLUS

CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(4-morpholinyl)-4-isoquinolinyl]phenyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 543734-92-5

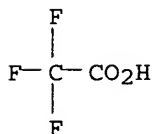
CMF C22 H26 Cl N3 O2



CM 2

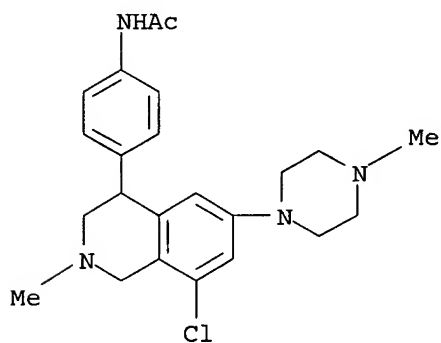
CRN 76-05-1

CMF C2 H F3 O2



RN 543737-73-1 HCAPLUS

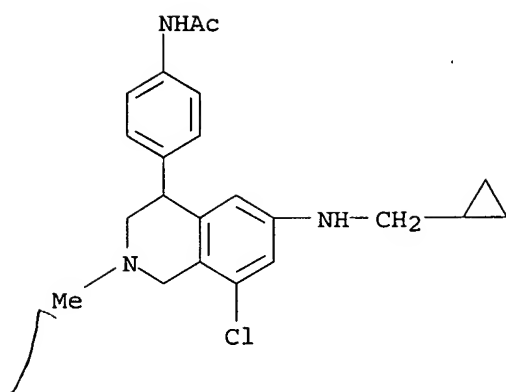
CN Acetamide, N-[4-[8-chloro-1,2,3,4-tetrahydro-2-methyl-6-(4-methyl-1-piperazinyl)-4-isoquinolinyl]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 543737-74-2 HCAPLUS

CN Acetamide, N-[4-[8-chloro-6-[(cyclopropylmethyl)amino]-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)

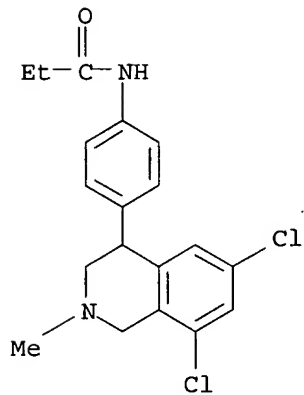


● x HCl

RN 543737-79-7 HCAPLUS
 CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

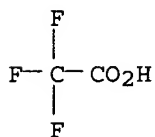
CM 1

CRN 543735-12-2
 CMF C19 H20 Cl2 N2 O



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

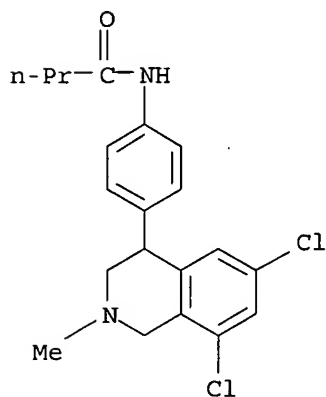


RN 543737-80-0 HCAPLUS
CN Butanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543735-14-4

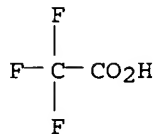
CMF C20 H22 Cl2 N2 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2

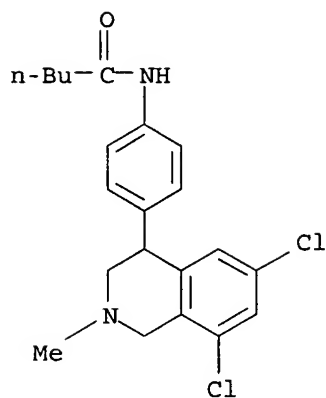


RN 543737-81-1 HCAPLUS
CN Pentanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543735-16-6

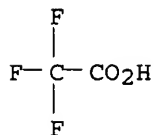
CMF C21 H24 Cl2 N2 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



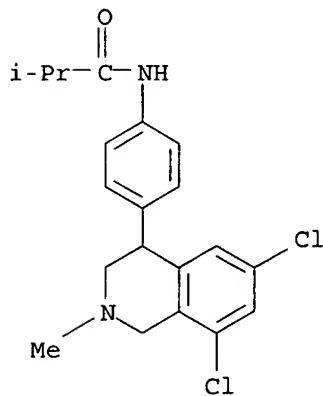
RN 543737-82-2 HCAPLUS

CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

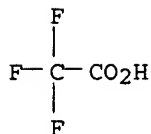
CRN 543735-17-7

CMF C20 H22 Cl2 N2 O



CM 2

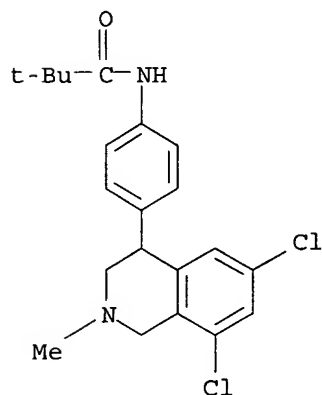
CRN 76-05-1
CMF C2 H F3 O2



RN 543737-83-3 HCAPLUS
CN Propanamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

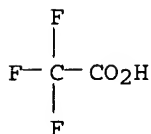
CM 1

CRN 543735-19-9
CMF C21 H24 Cl2 N2 O



CM 2

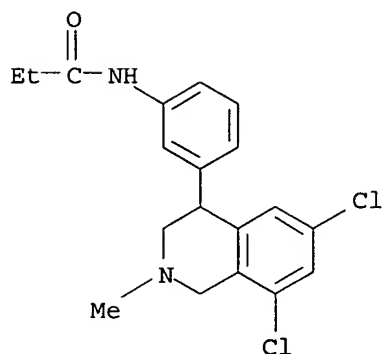
CRN 76-05-1
CMF C2 H F3 O2



RN 543737-90-2 HCAPLUS
CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

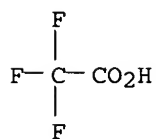
CM 1

CRN 543735-39-3
CMF C19 H20 Cl2 N2 O



CM 2

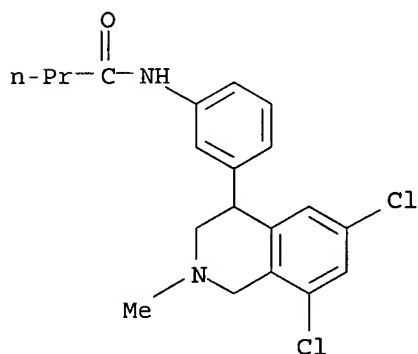
CRN 76-05-1
CMF C2 H F3 O2



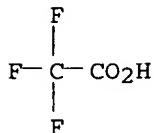
RN 543737-91-3 HCAPLUS
CN Butanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

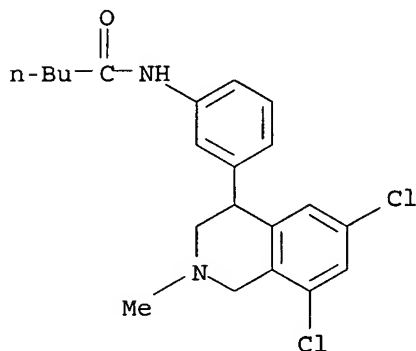
CRN 543735-41-7
CMF C20 H22 Cl2 N2 O



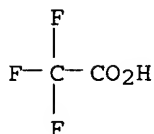
CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 543737-92-4 HCAPLUS
CN Pentanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

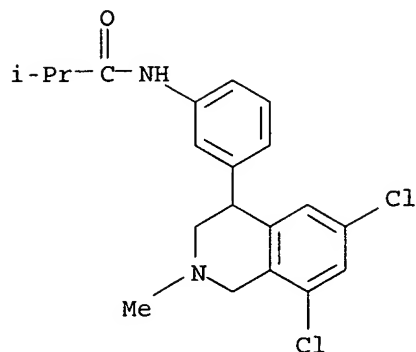
CRN 543735-42-8
CMF C21 H24 Cl2 N2 O

CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 543737-93-5 HCAPLUS
CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

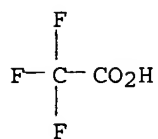
CM 1

CRN 543735-44-0
CMF C20 H22 Cl2 N2 O



CM 2

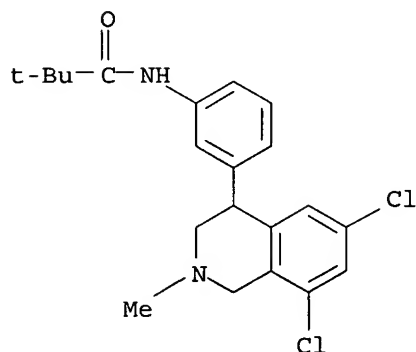
CRN 76-05-1
CMF C2 H F3 O2



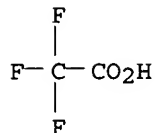
RN 543737-94-6 HCAPLUS
CN Propanamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

CM 1

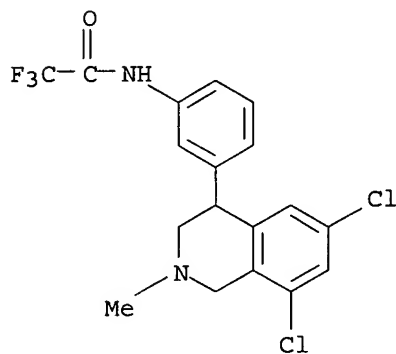
CRN 543735-46-2
CMF C21 H24 Cl2 N2 O



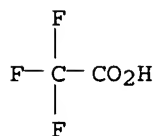
CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 543737-98-0 HCAPLUS
CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinoliny)phenyl]-2,2,2-trifluoro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

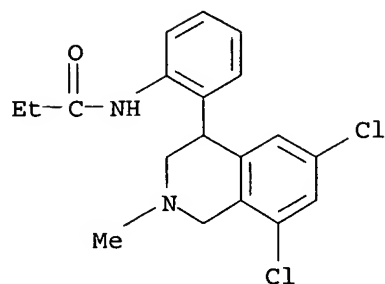
CRN 543735-54-2
CMF C18 H15 Cl2 F3 N2 O

CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 543738-04-1 HCAPLUS
CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinoliny)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

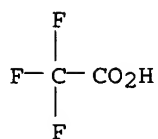
CM 1

CRN 543735-64-4
CMF C19 H20 Cl2 N2 O



CM 2

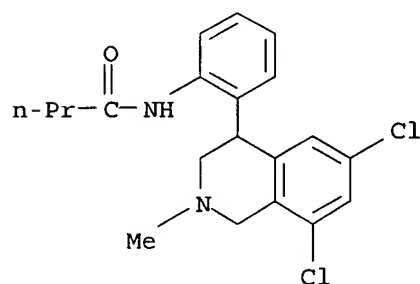
CRN 76-05-1
CMF C2 H F3 O2



RN 543738-05-2 HCAPLUS
CN Butanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

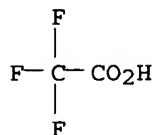
CM 1

CRN 543735-66-6
CMF C20 H22 Cl2 N2 O



CM 2

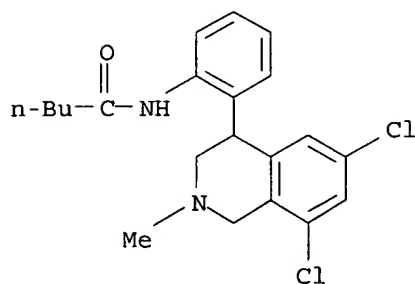
CRN 76-05-1
CMF C2 H F3 O2



RN 543738-06-3 HCAPLUS
 CN Pentanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

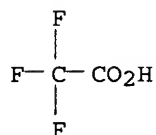
CM 1

CRN 543735-68-8
 CMF C21 H24 Cl2 N2 O



CM 2

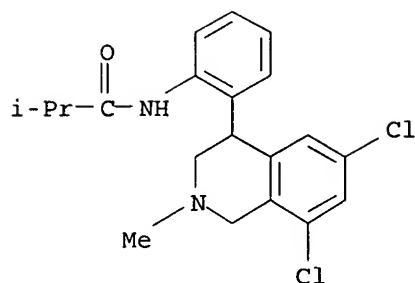
CRN 76-05-1
 CMF C2 H F3 O2



RN 543738-07-4 HCAPLUS
 CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-methyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

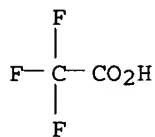
CRN 543735-69-9
 CMF C20 H22 Cl2 N2 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



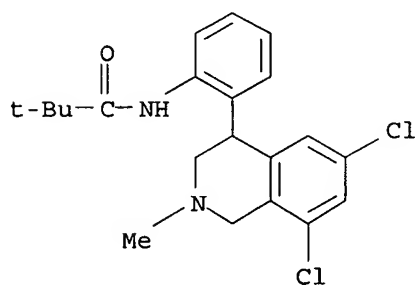
RN 543738-08-5 HCAPLUS

CN Propanamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2-dimethyl-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

CM 1

CRN 543735-71-3

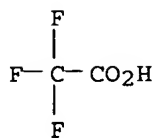
CMF C21 H24 Cl2 N2 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



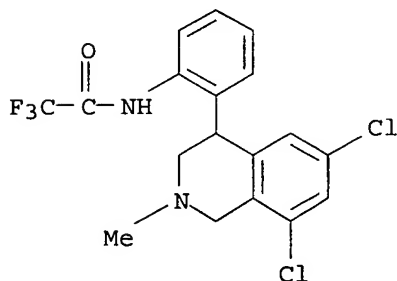
RN 543738-12-1 HCAPLUS

CN Acetamide, N-[2-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2,2-trifluoro-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 543735-76-8

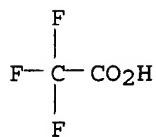
CMF C18 H15 Cl2 F3 N2 O



CM 2

CRN 76-05-1

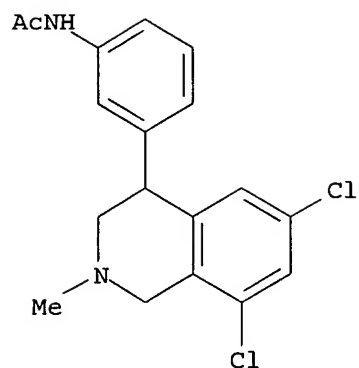
CMF C2 H F3 O2



RN 543738-23-4 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (-)-(9CI) (CA INDEX NAME)

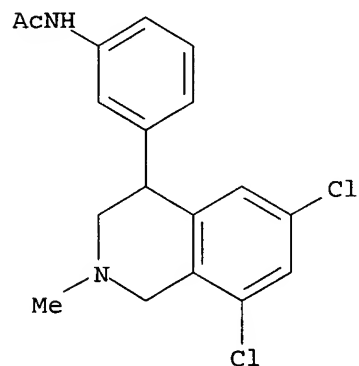
Rotation (-).



RN 543738-24-5 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (+)-(9CI) (CA INDEX NAME)

Rotation (+).



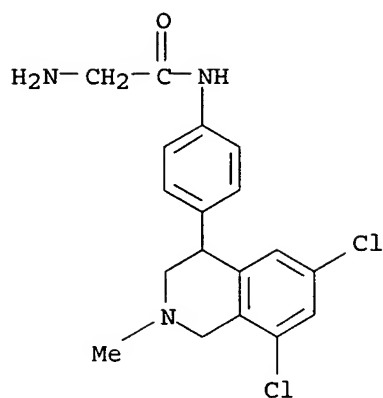
RN 543738-52-9 HCAPLUS

CN Acetamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543736-00-1

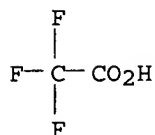
CMF C18 H19 Cl2 N3 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



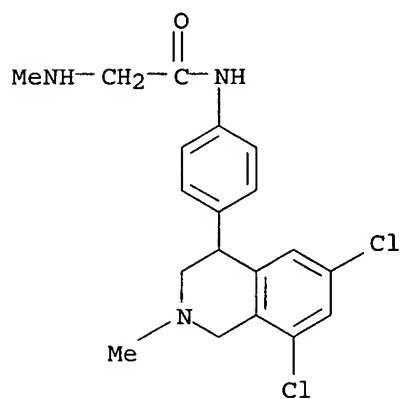
RN 543738-53-0 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinoliny)phenyl]-2-(methylamino)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

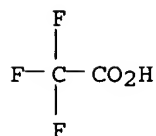
CRN 543736-01-2

CMF C19 H21 Cl2 N3 O



CM 2

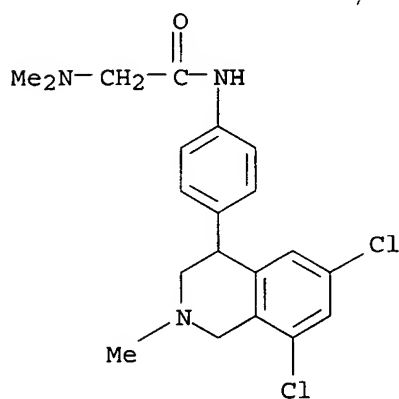
CRN 76-05-1
CMF C2 H F3 O2



RN 543738-54-1 HCAPLUS
CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(dimethylamino)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

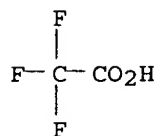
CM 1

CRN 543736-02-3
CMF C20 H23 Cl2 N3 O



CM 2

CRN 76-05-1
CMF C2 H F3 O2

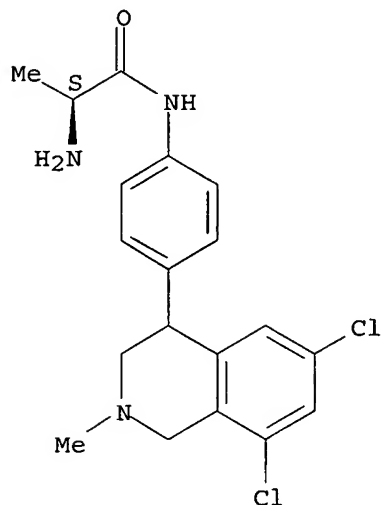


RN 543738-56-3 HCAPLUS
CN Propanamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

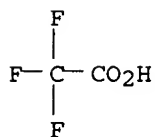
CRN 543738-55-2
CMF C19 H21 Cl2 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

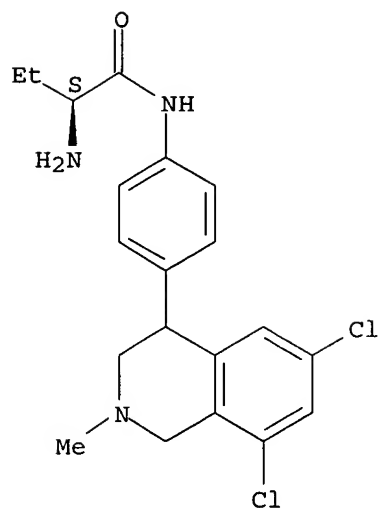


RN 543738-58-5 HCAPLUS
CN Butanamide, 2-amino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543738-57-4
CMF C20 H23 Cl2 N3 O

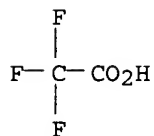
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 543738-60-9 HCAPLUS

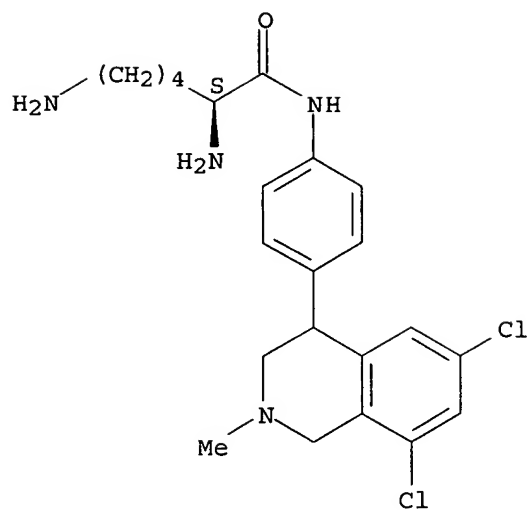
CN Hexanamide, 2,6-diamino-N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543738-59-6

CMF C22 H28 Cl2 N4 O

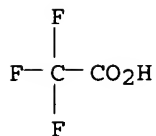
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



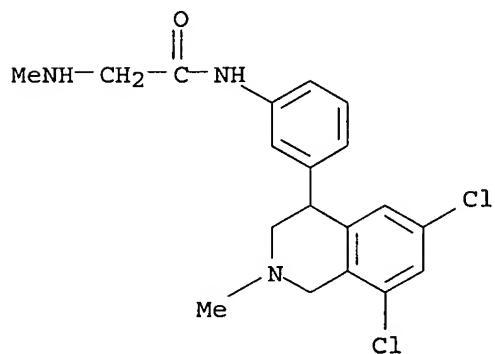
RN 543738-75-6 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinoliny)phenyl]-2-(methylanino)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543736-19-2

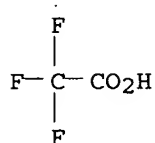
CMF C19 H21 Cl2 N3 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



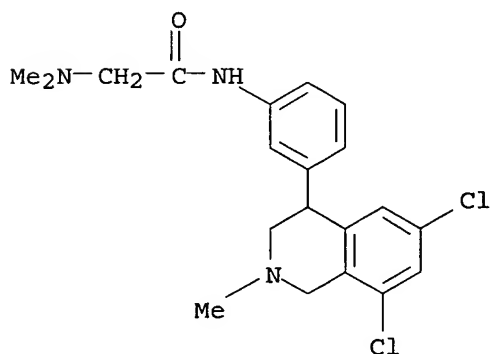
RN 543738-76-7 HCAPLUS

CN Acetamide, N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2-(dimethylamino)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 543736-20-5

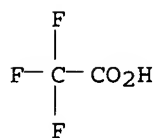
CMF C20 H23 Cl2 N3 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 543738-78-9 HCAPLUS

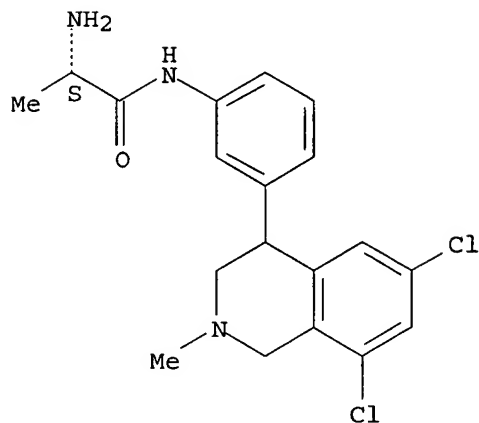
CN Propanamide, 2-amino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 543738-77-8

CMF C19 H21 Cl2 N3 O

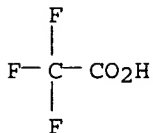
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 543738-80-3 HCAPLUS

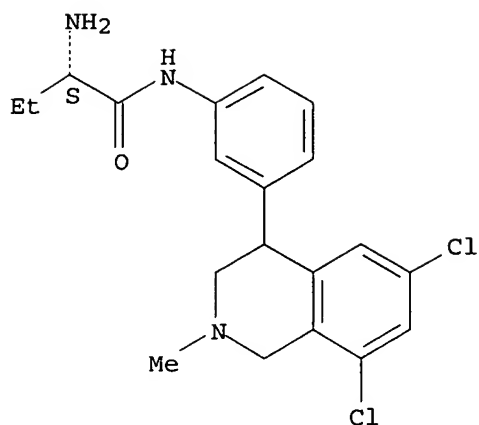
CN Butanamide, 2-amino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543738-79-0

CMF C20 H23 Cl2 N3 O

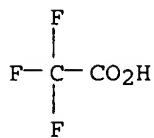
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 543738-82-5 HCAPLUS

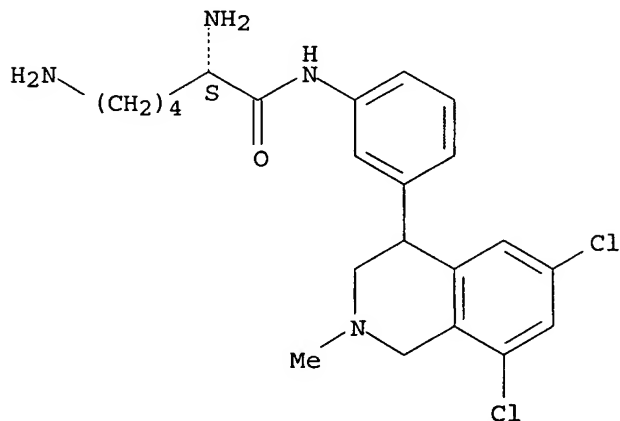
CN Hexanamide, 2,6-diamino-N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, (2S)-, mono(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 543738-81-4

CMF C22 H28 Cl2 N4 O

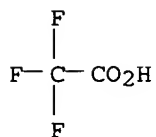
Absolute stereochemistry.



CM 2

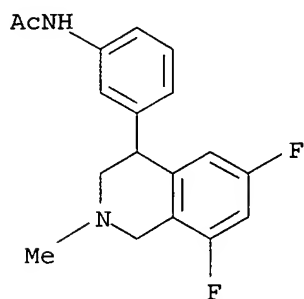
CRN 76-05-1

CMF C2 H F3 O2



RN 543739-80-6 HCAPLUS

CN Acetamide, N-[3-(6,8-difluoro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

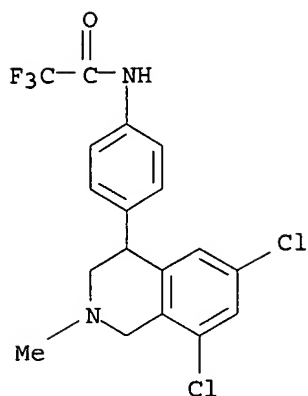
RN 543739-83-9 HCAPLUS

CN Acetamide, N-[4-(6,8-dichloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)phenyl]-2,2,2-trifluoro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 543735-27-9

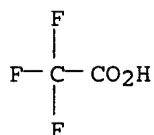
CMF C18 H15 Cl2 F3 N2 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IC ICM C07D217-22
ICS C07D401-12; C07D403-12; C07D417-12; C07D409-12; A61K031-47;
A61P009-12

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 24526-64-5P, 2-Methyl-4-phenyl-1,2,3,4-tetrahydroisoquinolin-8-ylamine 55774-26-0P, 4-(8-Amino-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenol 60520-18-5P, 5-(8-Amino-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-2-methoxyphenol 63806-80-4P, N-(2-Methyl-4-phenyl-1,2,3,4-tetrahydroisoquinolin-8-yl)acetamide 69275-19-0P, 4-(8-Amino-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzol-1,2-diol 69406-45-7P, 4-(3,4-Dichlorophenyl)-2-methyl-1,2,3,4-tetrahydroisoquinolin-8-ylamine 99087-42-0P 109086-13-7P 118411-63-5P 128942-68-7P 129010-57-7P 338999-84-1P 339001-35-3P **543734-46-9P**, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]acetamide 543734-48-1P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzenesulfonamide 543734-50-5P, 3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzenesulfonamide 543734-52-7P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N,N-dimethylbenzenesulfonamide 543734-54-9P 543734-56-1P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzoic acid 543734-58-3P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethylbenzamide 543734-60-7P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propylbenzamide 543734-62-9P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-(2-dimethylaminoethyl)benzamide 543734-64-1P 543734-66-3P

543734-68-5P 543734-70-9P 543734-72-1P 543734-74-3P
543734-76-5P, 4-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenylamine 543734-78-7P
543734-80-1P, 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-3-methylthiourea 543734-82-3P
543734-84-5P 543734-86-7P, N-[4-(2,6,8-Trimethyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]acetamide 543734-88-9P
, N-[4-(6-Bromo-8-chloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]acetamide 543734-90-3P 543734-92-5P
543734-94-7P, N-[4-[8-Chloro-2-methyl-6-(4-methylpiperazin-
1-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl]phenyl]acetamide
543734-96-9P, N-[4-[8-Chloro-6-(cyclopropylmethylamino)-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl]phenyl]acetamide
543734-98-1P, 5-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)-2-hydroxybenzoic acid 543735-00-8P,
5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-2-
hydroxy-N-methylbenzamide 543735-02-0P, 5-(6,8-Dichloro-2-methyl-
1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-2-hydroxybenzamide
543735-04-2P, 5-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)-N-(2-dimethylaminoethyl)-2-
hydroxybenzamide 543735-06-4P, N-[5-(6,8-Dichloro-2-methyl-
1,2,3,4-tetrahydroisoquinolin-4-yl)-2-hydroxybenzoyl]guanidine
543735-07-5P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]acetamide 543735-09-7P,
3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenylamine 543735-10-0P, 2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenylamine 543735-12-2P,
N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]propionamide 543735-14-4P,
N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]butyramide 543735-16-6P, Pentanoic
acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-17-7P, N-[4-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isobutyramide
543735-19-9P, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-2,2-dimethylpropionamide
543735-21-3P, Cyclopropancarboxylic acid-[4-(6,8-dichloro-2-methyl-
1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543735-23-5P,
Cyclobutancarboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-25-7P,
Cyclopentancarboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-27-9P
543735-29-1P, 1-Acetylpiperidin-4-carboxylic acid-[4-(6,8-dichloro-
2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide
543735-31-5P, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]nicotinamide 543735-33-7P,
N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]methansulfonamide 543735-35-9P, Ethansulfonic
acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-37-1P 543735-39-3P,
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]propionamide 543735-41-7P,
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]butyramide 543735-42-8P, Pentanoic
acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-44-0P, N-[3-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isobutyramide
543735-46-2P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-2,2-dimethylpropionamide
543735-48-4P, Cyclopropancarboxylic acid-[3-(6,8-dichloro-2-methyl-

1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543735-50-8P,
Cyclobutancarboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-52-0P,
Cyclopentancarboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-54-2P
543735-56-4P, 1-Acetylpiperidin-4-carboxylic acid-[3-(6,8-dichloro-
2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide
543735-58-6P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]nicotinamide 543735-60-0P,
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]methansulfonamide 543735-61-1P, Ethansulfonic
acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-62-2P 543735-64-4P,
N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]propionamide 543735-66-6P,
N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]butyramide 543735-68-8P, Pentanoic
acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-69-9P 543735-71-3P,
N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]-2,2-dimethylpropionamide 543735-73-5P,
Cyclopropanicarboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-74-6P,
Cyclobutancarboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-75-7P,
Cyclopentancarboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-76-8P
543735-77-9P, 1-Acetylpiperidin-4-carboxylic acid-[2-(6,8-dichloro-
2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide
543735-78-0P, N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]methansulfonamide
543735-79-1P, Ethansulfonic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-80-4P
543735-81-5P 543735-82-6P, 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-3-methylthiourea 543735-83-7P
543735-84-8P, 1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]-3-methylthiourea 543735-85-9P
543735-86-0P 543735-87-1P, 1,2-Dimethyl-1H-imidazole-4-sulfonic
acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-88-2P, 1,2-Dimethyl-1H-imidazole-4-
sulfonic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)phenyl]amide 543735-89-3P
543735-90-6P, 5-Chloro-1,3-dimethyl-1H-pyrazol-4-sulfonic
acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]amide 543735-91-7P 543735-92-8P 543735-93-9P
543735-94-0P 543735-95-1P 543735-96-2P 543735-97-3P
543735-98-4P, 2-Chloro-5-(6,8-dichloro-2-methyl-1,2,3,4-
tetrahydroisoquinolin-4-yl)benzenesulfonic acid amide
543735-99-5P, 2-Methyl-4-phenyl-6,8-bis(trifluoromethyl)-1,2,3,4-
tetrahydroisoquinolin 543736-00-1P, 2-Amino-N-[4-(6,8-
dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-
yl)phenyl]acetamide 543736-01-2P, N-[4-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2-
methylaminoacetamide 543736-02-3P, N-[4-(6,8-Dichloro-2-
methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2-
dimethylaminoacetamide 543736-03-4P,
2-Amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-
4-yl)phenyl]propionamide 543736-04-5P,
2-Amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-
4-yl)phenyl]butyramide 543736-05-6P, 2,6-Diaminohexanoic

acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-06-7P, Pyrrolidine-2-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-07-8P, N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isonicotinamide 543736-08-9P, 1H-Pyrrole-3-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-09-0P, 1H-Pyrrol-2-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-10-3P, 1-Methylpiperidin-4-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-11-4P, 1,4-Dimethyl-1H-pyrrol-2-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-12-5P, 4-Nitro-1H-pyrrol-2-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-13-6P, 2,5-Dimethyl-1H-pyrrol-3-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-14-7P, 1H-Imidazol-4-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-15-8P, 543736-16-9P, 3,5-Dimethyl-1H-pyrazol-4-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-17-0P, 1H-Pyrazol-4-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-18-1P, 3-Trifluoromethyl-1H-pyrazol-4-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-19-2P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2-methylaminoacetamide 543736-20-5P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-2-dimethylaminoacetamide 543736-21-6P, 2-Amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]propionamide 543736-22-7P, 2-Amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]butyramide 543736-23-8P, 2,6-Diaminohexanoic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-24-9P, Pyrrolidin-2-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-25-0P, N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]isonicotinamide 543736-26-1P, 1H-Pyrrol-3-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-27-2P, 1H-Pyrrol-2-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-28-3P, 1-Methylpiperidin-4-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-29-4P, 1,4-Dimethyl-1H-pyrrol-2-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-30-7P, 4-Nitro-1H-pyrrol-2-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-31-8P, 2,5-Dimethyl-1H-pyrrol-3-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-32-9P, 1H-Imidazol-4-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-33-0P, 543736-34-1P, 3,5-Dimethyl-1H-pyrazol-4-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-35-2P, 1H-Pyrazol-4-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-36-3P, 3-Trifluoromethyl-1H-pyrazol-4-

carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-37-4P,
1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-3-ethylthiourea 543736-38-5P, 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-3-ethylthiourea 543736-39-6P, 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]-3-ethylthiourea 543736-40-9P
543736-41-0P, 4-Methylpiperazin-1-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-42-1P, Piperidin-1-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-43-2P, Morpholin-4-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-44-3P, Pyrrolidin-1-carboxylic acid-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-45-4P 543736-46-5P 543736-47-6P 543736-48-7P
543736-49-8P 543736-50-1P 543736-51-2P 543736-52-3P 543736-53-4P 543736-54-5P 543736-55-6P 543736-56-7P
543736-57-8P, 4-Methylpiperazin-1-carboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-58-9P 543736-59-0P 543736-60-3P 543736-61-4P,
Piperidin-1-carboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-62-5P, Morpholin-4-carboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-63-6P,
Pyrrolidin-1-carboxylic acid-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-64-7P
543736-65-8P, 4-Methylpiperazin-1-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-66-9P, Pyrrolidin-1-carboxylic acid-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl]amide 543736-67-0P 543736-68-1P 543736-69-2P 543736-70-5P
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(drug candidate; preparation of phenyltetrahydroisoquinolines as sodium ion proton antiporter inhibitors)

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(drug candidate; preparation of phenyltetrahydroisoquinolines as sodium ion proton antiporter inhibitors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

=> fil marpat
FILE 'MARPAT' ENTERED AT 14:08:41 ON 25 AUG 2006

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L18 ANSWER 1 OF 6 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 145:8036 MARPAT
TITLE: Preparation of 4-phenyl substituted
tetrahydroisoquinolines and their use to block
reuptake of norepinephrine, dopamine, and
serotonin
INVENTOR(S): Molino, Bruce F.; Berkowitz, Barry; Cohen,
Marlene
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111393	A1	20060525	US 2004-994688	20041122
US 2006111396	A1	20060525	US 2005-284266	20051121
WO 2006057950	A2	20060601	WO 2005-US42110	20051121

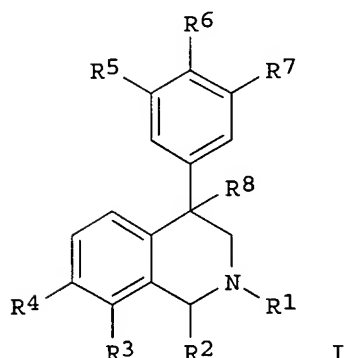
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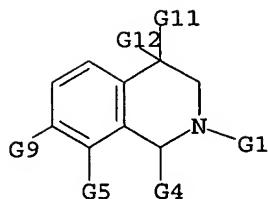
US 2004-994688 20041122

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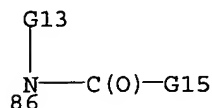


AB The invention is related to a method of treating disorders including stress urinary incontinence, migraine, and neuropathic pain by administering to a patient in need of such treatment a therapeutically effective amount of a disclosed compound of formula (I) [R1 = (un)substituted alk(en/yn)yl, cycloalkyl/alkyl; R2 = H, alk(en/yn)yl, haloalkyl, etc.; R3, R4 = independently H, halo, OH and derivs., cyclo/alkyl, etc.; R5-R7 = independently H, NHCONH-alkyl and derivs., NH2 and derivs., etc.; R8 = H, halo, OH and derivs.; with provisos]. The invention is also related to the preparation of 4-Ph substituted tetrahydroisoquinolines I and analogs. E.g., reductive alkylation of m-methylbenzaldehyde with α -[(methylamino)methyl]benzyl alc. and cyclization in DCM in the presence of 98% H₂SO₄ gave 2,7-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline. I are more selective for the norepinephrine transporter (NET) protein than the dopamine transporter (DAT) protein or serotonin transporter (SERT) proteins. Generally, I have a Ki ratio for DAT/NET and SERT/NET of at least about 2:1 and 20:1, resp.

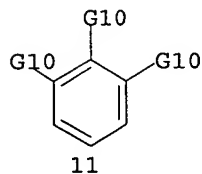
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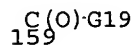
G1 = Me
G5 = F
G10 = 86



G11 = 11



G15 = 159



Patent location: claim 1
Note: substitution is restricted
Note: or oxides, pharmaceutically acceptable salts, solvates, or prodrugs
Stereochemistry: 7 - R or S

L18 ANSWER 2 OF 6 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:488538 MARPAT
TITLE: Preparation of hetero/aryl substituted tetrahydroisoquinolines and their use to block reuptake of norepinephrine, dopamine and serotonin
INVENTOR(S): Molino, Bruce F.; Berkowitz, Barry; Cohen, Marlene
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2006111394 A1 20060525 US 2004-994956 20041122
 US 2006111395 A1 20060525 US 2005-284264 20051121
 WO 2006058016 A2 20060601 WO 2005-US42347 20051121

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 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
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 NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL,
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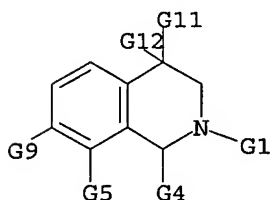
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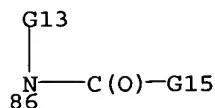
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT
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AB The invention is related to a method of treating disorders including stress urinary incontinence, migraine, and neuropathic pain by administering to a patient in need of such treatment a therapeutically effective amount of a disclosed compound of formula (I) [R1 = (un)substituted alk(en/yn)yl, cycloalkyl/alkyl; R2 = H, alk(en/yn)yl, cycloalkyl/alkyl, haloalkyl; R3 = H, halo, OH and derivs., CN, alkyl, etc.; R4 = (un)substituted Ph, naphthyl, indenyl, pyrimidinyl, benzofuranyl, etc.; R5-R7 = independently H, halo, OH and derivs., CN, SH and derivs., (un)substituted alk(en/yn)yl, etc.; or R5CCR6 = -O-(CH2)2-O- and derivs.; R8 = H, halo, OH and derivs.]. The invention is also related to the preparation of 4-Ph substituted tetrahydroisoquinolines I, stereoisomers, and analogs. E.g., a 5-step synthesis starting from 3-iodobenzyl alc. was given for tetrahydroisoquinoline II. I are more selective for the norepinephrine transporter (NET) protein than the dopamine transporter (DAT) protein or serotonin transporter (SERT) proteins. Generally, I have a Ki ratio for DAT/NET and SERT/NET of at least about 2:1 and 20:1, resp.

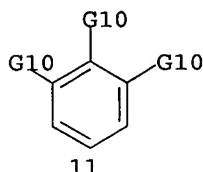
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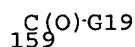
G1 = Me
 G5 = F
 G10 = 86



G11 = 11



G15 = 159



Patent location: claim 1
 Note: substitution is restricted
 Note: or oxides, pharmaceutically acceptable salts, solvates, or prodrugs
 Stereochemistry: 7 - R or S

L18 ANSWER 3 OF 6 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 141:33822 MARPAT

TITLE: The use of aryl- and heteroaryl-substituted tetrahydroisoquinolines in the treatment of chronic and neuropathic pain, migraine headaches, and urge, stress and mixed urinary incontinence

INVENTOR(S): Frail, Donald Edward; Arneric, Stephen Peter; Wishka, Donn Gregory; Wong, Erik Ho Fong; Beck, James Peter

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050630	A1	20040617	WO 2003-IB5504	20031124
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,				

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
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AU 2003283646 A1 20040623 AU 2003-283646 20031124

US 2004248932 A1 20041209 US 2003-724856 20031201

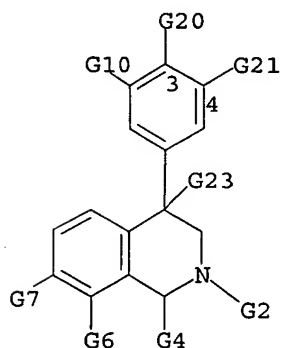
PRIORITY APPLN. INFO.:

US 2002-430285P 20021202

WO 2003-IB5504 20031124

AB Methods are disclosed for using aryl- and heteroaryl-substituted tetrahydroisoquinolines for the treatment of chronic and neuropathic pain, the treatment and prevention of migraine headache, and the treatment of stress, urge and mixed urinary incontinence.

MSTR 1



G2 = Me

G6 = F

G10 = 41

G11-G12
41

G11 = 43

N-G13
43

G13 = 47

C(O)-G15
47

G15 = CH₂Ph (opt. substd.)

G20 = 68

G11-G12
68

G21 = 79

G11-G12
79

Patent location: claim 1
Note: or pharmaceutically acceptable salts or
prodrugs
Stereochemistry: or isomers
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L18 ANSWER 4 OF 6 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 141:33820 MARPAT

TITLE: The use of 4-phenyl-substituted
tetrahydroisoquinolines in the treatment of
pain, migraine headaches and urinary
incontinence

INVENTOR(S): Frail, Donald Edward; Arneric, Stephen Peter;
Wishka, Donn Gregory; Wong, Erik Ho Fong;
Beck, James Peter

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

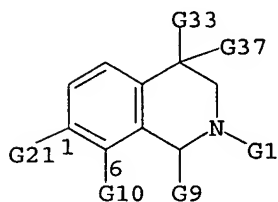
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050628	A1	20040617	WO 2003-IB5339	20031120
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CA 2505783	AA	20040617	CA 2003-2505783	20031120
AU 2003280137	A1	20040623	AU 2003-280137	20031120
EP 1572658	A1	20050914	EP 2003-772511	20031120
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BR 2003016919	A	20051018	BR 2003-16919	20031120
JP 2006509782	T2	20060323	JP 2004-556621	20031120
US 2004248933	A1	20041209	US 2003-724857	20031201
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			WO 2003-IB5339	20031120

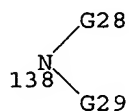
AB .Methods are disclosed for using aryl- and heteroaryl-substituted tetrahydroisoquinolines, for the treatment of chronic and neuropathic pain, the treatment and prevention of migraine

headache, and the treatment of stress, urge and mixed urinary incontinence.

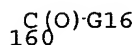
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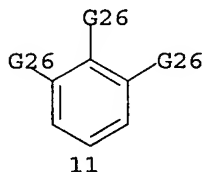
G1 = Me
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 G16 = CH₂Ph (opt. substd.)
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G29 = 160



G33 = 11



Patent location: claim 1
 Note: substitution is restricted
 Note: or oxides, pharmaceutically acceptable salts, solvates or prodrugs

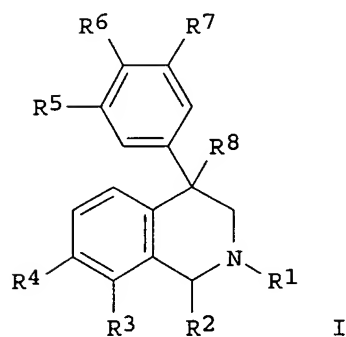
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 6 MARPAT COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 134:353258 MARPAT
 TITLE: Aryl- and heteroaryl-substituted tetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin
 INVENTOR(S): Beck, James P.; Curry, Matt A.; Smith, Mark A.
 PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
 SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032625	A1	20010510	WO 2000-US30329	20001103
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2389306	AA	20010510	CA 2000-2389306	20001103
BR 2000015320	A	20020709	BR 2000-15320	20001103
EP 1246806	A1	20021009	EP 2000-976885	20001103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
JP 2003513074	T2	20030408	JP 2001-534777	20001103
AU 781179	B2	20050512	AU 2001-14597	20001103
US 2002143014	A1	20021003	US 2002-91949	20020306
US 6579885	B2	20030617		
US 2003203920	A1	20031030	US 2003-426097	20030429
US 2005020597	A1	20050127	US 2004-917801	20040813
PRIORITY APPLN. INFO.:				
			US 1999-163269P	19991103
			US 2000-704305	20001102
			WO 2000-US30329	20001103
			US 2002-91949	20020306
			US 2003-426097	20030429

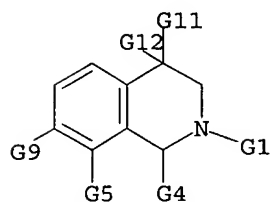
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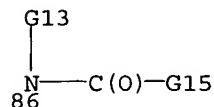
AB Diarylmethyltetrahydroisoquinolines (4R)- or (4S)-I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3 = H, halogen, (un)substituted OH, S(O)nH, CN, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R4 = (un)substituted aryl, heteroaryl; R5-R7 = H, halogen, CN, (un)substituted OH, NH2, S(O)nH, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, (un)substituted OH; n = 0-2] prepared for use as blockers of the reuptake of norepinephrine, dopamine and serotonin (no data). Thus, 3-bromobenzaldehyde is stirred in the presence of

methylamine and reduced with sodium borohydride followed by addition of α -chloroacetophenone and reduction of the amino ketone in situ with sodium borohydride to give 3-BrC₆H₄CH₂N(Me)CH₂CH(OH)Ph; cyclization of the benzyl alc. with sulfuric acid followed by coupling with phenylboronic acid gave I (R₁ = Me; R₄ = Ph; R₂ = R₃ = R₅ = R₆ = R₇ = H) as an oil. Such compds. are particularly useful in the treatment of a neurol. and psychiatric disorders which are created by or are dependent upon decreased availability of serotonin, norepinephrine or dopamine, such as attention deficit-hyperactivity disorder (ADHD), anxiety, depression, and addiction disorders.

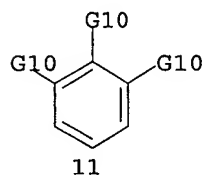
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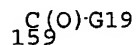
G1 = Me
G5 = F
G10 = 86



G11 = 11



G15 = 159



Patent location:

Note:

Note:

Stereochemistry:

REFERENCE COUNT:

claim 1

substitution is restricted

or oxides, pharmaceutically acceptable

salts, solvates, or prodrugs

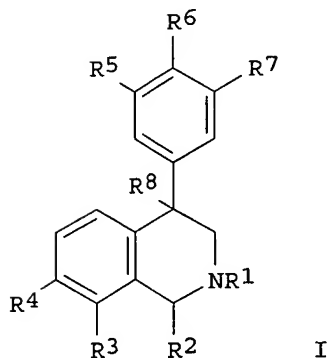
7 - R or S

8 THERE ARE 8 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L18 ANSWER 6 OF 6 MARPAT COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 134:353257 MARPAT
 TITLE: 4-Phenyltetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin
 INVENTOR(S): Beck, James P.; Smith, Mark A.
 PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
 SOURCE: PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032624	A1	20010510	WO 2000-US30328	20001103
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2389300	AA	20010510	CA 2000-2389300	20001103
BR 2000015307	A	20020709	BR 2000-15307	20001103
EP 1246805	A1	20021009	EP 2000-976884	20001103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
JP 2004501860	T2	20040122	JP 2001-534776	20001103
NZ 519146	A	20040227	NZ 2000-519146	20001103
AU 784280	B2	20060302	AU 2001-14596	20001103
PRIORITY APPLN. INFO.:			US 1999-163270P	19991103
			WO 2000-US30328	20001103

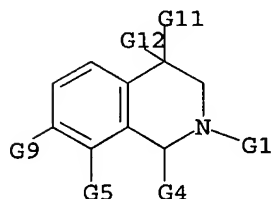
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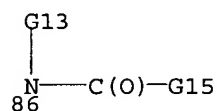
AB Tetrahydroisoquinolines I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3-R7 = H, halogen, (un)substituted OH, S(O)nH, S(O)nNH₂, CN, acyl, CONH₂, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, halogen, (un)substituted OH] were prepared for use as inhibitors of the uptake of norepinephrine, dopamine and serotonin in the treatment of various neurol. and psychiatric

disorders, e.g. ADHD (no data). Thus, 3-MeC₆H₄CHO was reductively alkylated with HOCHPhCH₂NHMe and cyclized with 98% H₂SO₄ to give 2,7-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline.

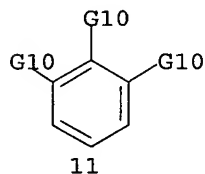
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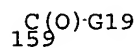
G1 = Me
G5 = F
G10 = 86



G11 = 11



G15 = 159



Patent location:

Note:

Note:

Stereochemistry:

claim 1

substitution is restricted

or oxides, pharmaceutically acceptable

salts, solvates, or prodrugs

7 - R or S

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT